

2026

RePCORT

I N D I A

ANNUAL JOINT LEADERSHIP MEETING

HOSTED BY
**Jawaharlal Institute of Postgraduate
Medical Education & Research (JIPMER)**
Puducherry, India
July 29-31, 2026

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PARTICIPATING INSTITUTIONS

- Bhagwan Mahavir Medical Research Center (BMMRC)
- Byramjee Jeejeebhoy Government Medical College (BJGMC)
- Byramjee Jeejeebhoy Government Medical College (BJGMC)-Johns Hopkins University (JHU) Clinical Research Site (BJGMC-JHU CRS)
- Boston University/Boston Medical Center (BU/BMC)
- Christian Medical College, Vellore (CMC)
- Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER)
- Johns Hopkins University (JHU)
- Prof. M. Viswanathan Diabetes Research Centre (MVDRC)
- National Institute for Research In Tuberculosis (NIRT)
- National Institute for Research In Tuberculosis (NIRT) – International Centers for Excellence in Research (ICER)
- North Eastern Indira Gandhi Regional Institute of Health & Medical Sciences (NEIGRIHMS)
- P.D. Hinduja National Hospital and Medical Research Centre (Hinduja)
- Postgraduate Institute of Medical Education and Research (PGI), Chandigarh
- Rutgers University
- St. Louis University School of Medicine (SLU)
- University of Massachusetts (UMass)

SPECIALIZED LABS & COLLABORATORS

- All Indian Institute of Medical Sciences (AIIMS), New Delhi, India
- Cornell University, New York, USA
- Emory University, Georgia, USA
- Fundação Oswaldo Cruz (FIOCRUZ), Bahia, Brazil
- Imperial College, London, UK
- Indian Institute of Science (IISc), Bengaluru, India
- Indian Institute of Science and Education (IISER), Pune, India
- Indian Institute of Technology Bombay (IIT-B) – Proteomics Core, Mumbai, India
- Medgenome, Bengaluru, India
- National Center for Functional Glycomics, Massachusetts, USA
- National Institute of Immunology (NII), Delhi, India
- Office of Cyber Infrastructure and Computational Biology (NIAID), Maryland, USA
- South African TB Vaccine Initiative (SATVI), Cape Town, South Africa
- theraCUES Innovation Pvt Ltd, Bengaluru, India
- Translational Health Science and Technology Institute (THSTI), Faridabad, India
- University of California—San Francisco (UCSF)

SPONSORS

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RePORT
INDIA

14th RePORT India Annual Meeting
10th to 12th April 2025
Venue - CSIR-CCMB

RePCORT

INDIA

OVERVIEW



Background

RePORT (Regional Prospective Observational Research for Tuberculosis) India is a bilateral, multi-organizational, collaborative research effort established in 2013 under the Indo-US Vaccine Action Program (VAP). RePORT India is now the largest of six regional consortia—China, Brazil, Indonesia, Philippines, and South Africa are also undertaking multi-organizational tuberculosis (TB) research efforts. Each RePORT consortium is designed to support local, in-country, TB-specific data and specimen biorepositories and associated research. Taken together, the anticipated results include greater global clinical research capacity in high-burden settings and increased local access to quality data and specimens for members of each consortia and their domestic and international collaborators. Leveraging the data, specimens, infrastructure, and scientific partnerships established by RePORT India in Phase 1 (2013-2018), the consortium has now launched Phase II (2019-2026).

Mission

RePORT India is charged with:

1. Advancing regional TB science in India, towards fulfilling the TB strategic goals of the country;
2. Strengthening TB research capacity and infrastructure; and
3. Fostering research collaboration within India and with other countries focused on research that can lead to clinically important biomarkers, vaccines, drugs, and diagnostics.

Phase 1 – Parent Protocols

Phase I (2013–18) commenced with six Clinical Research Sites (CRSs) in Western and Southern India that were partnered with five U.S. academic institutions. P.D. Hinduja National Hospital and Medical Research Centre was subsequently added as the seventh Indian site. Initially, each site had its own “Parent Protocol” with distinct research topics. Clinical, behavioral, radiological and biological samples were collected from the enrollees, including sputum, blood, urine etc. The specimens were stored at the ICMR-NIRT biobank for scientific analysis. TB patients and their household contacts were followed for a period of two years.

Cohort A: Participants who have active TB disease. Studies involving this cohort of patients focused on TB diagnosis and treatment outcomes.

- **2455** patients enrolled with TB inside the lungs (including 133 with drug-resistant TB)
- **588** patients enrolled with TB outside the lungs
- **207** children enrolled with TB

Cohort B: Participants who are household contacts (HHCs) of an active case of TB. Studies involving this cohort of participants focused on risk of infection and progression to TB disease after exposure.

- **3766** HHCs of coughing adult patients with TB inside the lungs enrolled

BMMRC & SLU

- **Topic of Study:** Immunologic Markers of Persons at Highest Risk of Progression of Latent TB Infection to TB
- **India PI:** Dr. Vijaya Valluri, Bhagawan Mahavir Medical Research Centre (BMMRC), Hyderabad, India
- **U.S. PI:** Dr. Krishna Vankayalapati, St Louis University School of Medicine, St. Louis, MO, USA
- **Participating Patient Cohort:** Cohort B

- **Design:** This prospective longitudinal observational cohort study follows 1,000 household contacts of pulmonary TB patients for two years to identify immunologic biomarkers associated with progression from latent tuberculosis infection (LTBI) to active tuberculosis. Participants undergo serial clinical evaluations and blood collection every four months to characterize immune responses predictive of disease progression.
- **Aims:**
 1. Determine whether monocyte phenotype and function predict progression from latent TB infection to active tuberculosis.
 2. Determine whether natural killer (NK) cell phenotype and function predict progression to active tuberculosis.
 3. Determine whether regulatory T-cell (Treg) numbers, immunosuppressive function, and antimicrobial activity identify individuals at highest risk for developing active tuberculosis.

BJGMC, NIRT, & JHU

- **Topic of Study:** Host and Microbial Factors Associated with Poor Treatment Response and Progression to Active TB (C-TRIUMPH)
- **India PIs:** Drs. Sanjay Gaikwad, Aarti Kinikar, Rajesh Karyakarte, Byramjee Jeejeebhoy Government Medical College (BJGMC), Pune, India; Dr. Vidya Mave, Mandar Paradkar, BJGMC-JHU CRS, Pune, India; Drs. Bhavani PK, Luke Elizabeth Hanna, National Institute for Research in TB (NIRT), Chennai, India
- **U.S. PI:** Dr. Amita Gupta, Johns Hopkins University, Baltimore, MD, USA
- **Participating Patient Cohorts:** Cohort A (Adult Pulmonary TB, Pediatric TB, and Extrapulmonary TB) and Cohort B'
- **Design:** This multicenter prospective observational cohort study was established to investigate the host, microbial, environmental, and behavioral determinants of tuberculosis treatment outcomes, disease progression, and transmission. Cohort A participants were followed for 24 months to evaluate treatment response, recurrence, and post-treatment outcomes, while Cohort B household contacts were followed for 24 months to identify incident TB, progression from infection to active disease, and transmission dynamics. Comprehensive clinical, epidemiologic, imaging, pulmonary function, and biospecimen data were collected longitudinally to support translational research.
- **Aims:**
 1. Determine the host and microbial factors associated with tuberculosis treatment outcomes.
 2. Investigate host and microbial determinants of progression from TB infection to active disease.
 3. Characterize tuberculosis transmission dynamics and establish a comprehensive clinical database and biorepository to support future biomarker, immunologic, genomic, and translational research.

CMC Vellore & U of Wash/U of Cambridge

- **Topic of Study:** Host Determinants in the Eicosanoid Pathway that Modulate the Inflammatory Response, Disease Outcome, and Treatment Responsiveness in TB
- **India PI:** Drs. DJ Christopher and Balamugesh Thangakunam, Christian Medical College (CMC), Vellore, India

- **U.S. PI:** Dr. Lalitha Ramakrishnan, University of Washington/University of Cambridge, UK
- **Participating Patient Cohort:** Cohort A (Adult Pulmonary TB and TB Meningitis)
- **Design:** This is a prospective observational cohort study evaluating host genetic determinants of inflammation and their association with disease severity, treatment response, and clinical outcomes among adults with pulmonary tuberculosis and tuberculosis meningitis receiving standard-of-care anti-tuberculosis therapy.
- **Aims:**
 1. Determine whether host genetic variants in the LTA4H/eicosanoid pathway are associated with inflammatory responses, disease severity, and treatment outcomes in pulmonary tuberculosis and tuberculosis meningitis.
 2. Evaluate whether hyper-inflammatory or hypo-inflammatory LTA4H genotypes and other TNF-associated genetic variants influence sputum smear and culture conversion in pulmonary tuberculosis.
 3. Assess the relationship between host genotypes, cerebrospinal fluid inflammatory markers (including lipoxin A4 and leukotriene B4), and mortality among patients with tuberculosis meningitis receiving adjunctive corticosteroid therapy.
 4. Investigate whether genetic variants associated with enhanced necroptosis pathways contribute to delayed treatment response and increased mortality following *Mycobacterium tuberculosis* infection.

Hinduja & JHU

- **Topic of Study:** MDR-TB Treatment Outcomes, Adverse Effects, Mtb Genotyping, and Pharmacokinetic Testing
 - **India PIs:** Drs. Zarir F. Udwadia, Tester F. Ashavaid, and Camilla Rodrigues; P.D. Hinduja National Hospital and Medical Research Centre, Mumbai, India
 - **U.S. PIs:** Drs. Amita Gupta and Jeffrey Tornheim, Johns Hopkins University (JHU), Baltimore, MD, USA
 - **Participating Patient Cohorts:** Cohort A (Adult/Adolescent MDR-TB) and Cohort B
- **Topic of Study:** Predictors of Resistance Emergence Evaluation in Multidrug Resistant-Tuberculosis Patients on Treatment (PREEMPT)
 - **India PIs:** Drs. Zarir F. Udwadia, Tester F. Ashavaid, and Camilla Rodrigues; P.D. Hinduja National Hospital and Medical Research Centre, Mumbai, India
 - **U.S. PIs:** Drs. Robert Horsburgh, Boston University, Boston, MA, USA; Dr. Timothy Sterling, Vanderbilt University, Nashville, TN, USA
 - **Participating Patient Cohorts:** Adult PTB MDR patients on TB treatment
- **Design:** In this observational cohort study, we propose to study the contribution of potential causes to resistance and develop the knowledge base required to stop resistance from developing by analyzing AUC and sputum samples.
- **Aims:**
 1. Determine whether low serum antimycobacterial drug concentrations are associated with the clinical emergence of drug resistance in MDR-TB patients.
 2. Determine whether HIV seropositivity is a risk factor for low serum drug concentrations.
 3. Determine the contribution of increased DNA mutation to clinical emergence of drug resistance in patient isolates.
 4. Determine the earliest time at which mutations responsible for drug resistance can be detected during treatment.

JIPMER, BU/BMC, & Rutgers

- **Topic of Study:** Biomarkers for Risk of TB and for TB Treatment Failure and Relapse
- **India PIs:** Drs. Gautam Roy and Sonali Sarkar, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India
- **U.S. PIs:** Drs. Jerrold Ellner and Padmini Salgame, Rutgers University, Newark, NJ, USA; Dr. Robert Horsburgh, Boston University (BU), Boston, MA, USA; Dr. Natasha Hochberg, Boston Medical College (BMC), Boston, MA, USA
- **Participating Patient Cohorts:** Cohort A (Adult Pulmonary TB and Pediatric TB) and Cohort B
- **Design:** This prospective observational cohort study established two longitudinal cohorts: a pulmonary tuberculosis index case cohort and a household contact cohort. Participants underwent detailed clinical assessments, biospecimen collection, transcriptomic analyses, and longitudinal follow-up to identify biomarkers predictive of tuberculosis treatment failure, relapse, and progression from latent TB infection to active disease. The study also evaluated the influence of major co-morbidities—including diabetes mellitus, HIV, helminth infection, malnutrition, smoking, alcoholism, and anemia—on TB outcomes.
- **Aims:**
 1. Identify biomarkers predictive of tuberculosis treatment failure in pulmonary TB patients.
 2. Identify biomarkers predictive of progression from household exposure to active tuberculosis.
 3. Determine the impact of major co-morbidities on tuberculosis treatment outcomes, latent TB infection, and progression to active disease.
 4. Characterize transcriptomic and immune network profiles associated with treatment failure and progression from latent to active tuberculosis.

MVDRC, NIRT-ICER, & UMass

- **Topic of Study:** Effects of Diabetes and Prediabetes on TB Severity
- **India PIs:** Dr. Vijay Viswanathan, MV Diabetes Research Centre (MVDRC), Chennai, India; Dr. Subash Babu, National Institute for Research In Tuberculosis (NIRT) – International Centers for Excellence in Research (ICER), Chennai, India
- **U.S. PI:** Dr. Hardy Kornfeld, University of Massachusetts (UMass) Medical School, Boston, USA
- **Participating Patient Cohort:** Cohort A (Adult Pulmonary TB)
- **Design:** This prospective observational cohort study investigates the impact of diabetes mellitus on the clinical presentation, treatment response, and long-term outcomes of pulmonary tuberculosis. Newly diagnosed pulmonary TB patients with and without diabetes are enrolled and followed throughout TB treatment and for one year after treatment completion to evaluate disease severity, sputum conversion, treatment outcomes, relapse, and immunologic mechanisms.

MVDRC, NIRT-ICER, & UMass

Aims:

1. Determine whether diabetes mellitus is associated with increased severity of pulmonary tuberculosis at presentation, including radiographic severity and sputum smear/culture burden.
2. Evaluate the effect of diabetes on treatment response, including time to sputum smear and culture conversion and anti-TB treatment outcomes (failure, death, and relapse).
3. Investigate the relationship between diabetes severity (HbA1c and clinical severity score) and tuberculosis disease severity and outcomes.
4. Characterize the immunologic and transcriptional mechanisms underlying the interaction between diabetes and tuberculosis to identify biomarkers associated with disease progression and treatment response.

Phase 1 – Common Protocol

Based on the tremendous productivity of RePORT India's Phase I identifying new blood-based, sputum-based and urine-based biomarkers that can diagnose TB, or predict TB patients' treatment success or failure or death, and for assessing new vaccines to prevent getting TB again (relapse) for those starting TB treatment, the governments of India and the US bilaterally funded the extension of Phase I in to a "Common Protocol" in 2017. The Common Protocol allowed for standardized data elements and harmonized procedures for enrollment across all sites to 1) identify newer, more accurate biomarkers and 2) confirm the utility of previously discovered biomarkers by validating them on samples stored in the ICMR-NIRT sample bank. The Common Protocol enrolled and followed TB patients and their HHCs for a period of two years.

Cohort A: Participants who have active TB disease.

- **724** adult patients enrolled with TB inside the lungs

Cohort B: Participants who are household contacts (HHCs) of an active case of TB.

- **898** household contacts of coughing adult patients with TB inside the lungs enrolled

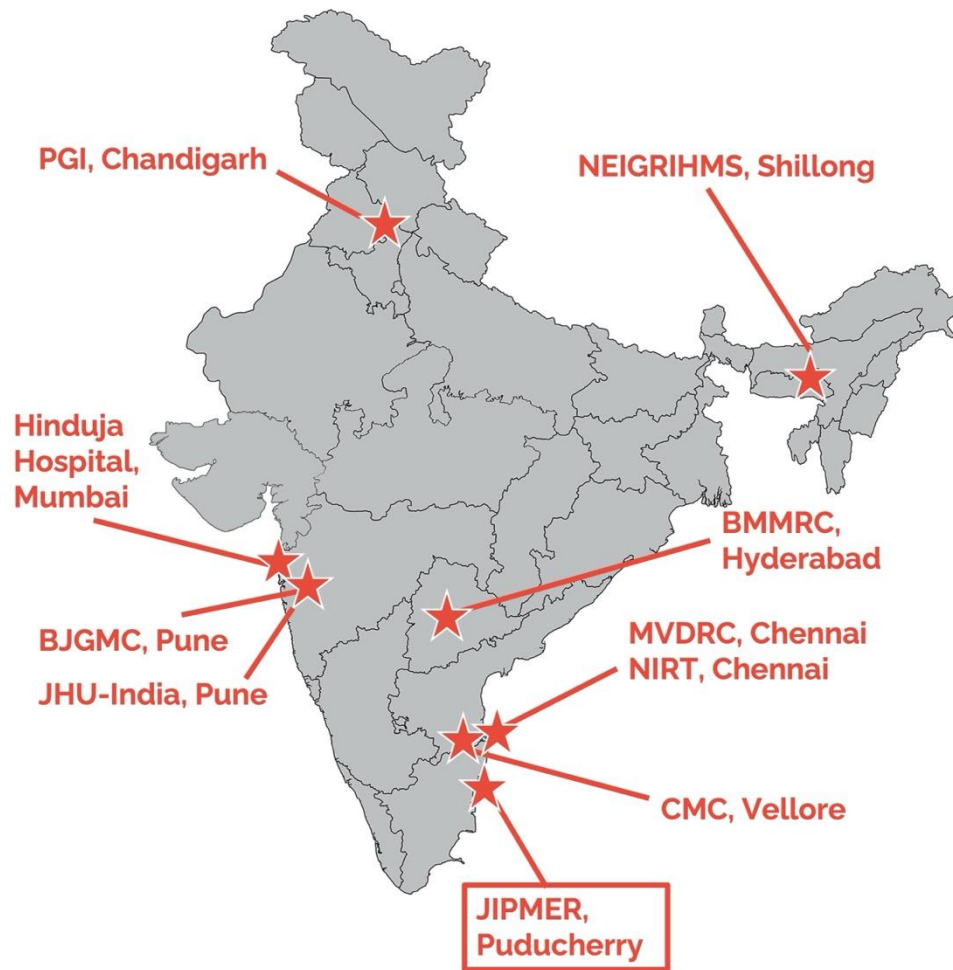
Phase 1 – Achievements

- **106** scientific publications to advance TB science and public health
- **64** new projects utilizing the collected and stored samples for new biomarkers
- **245** presentations to showcase the work done in the RePORT Consortium
- New child TB diagnosis and treatment response gene-signatures unique for India
- New Transcriptomic, Lipidomic and Metabolomic signatures as blood biomarkers
- New vaccine trials to prevent TB relapse, Clinical biomarkers of TB death and relapse
- Key public health finding that informed the country's National TB Elimination Program guideline policies and more public health findings in the list with potential to guide further.

Phase 2 – Common Protocol

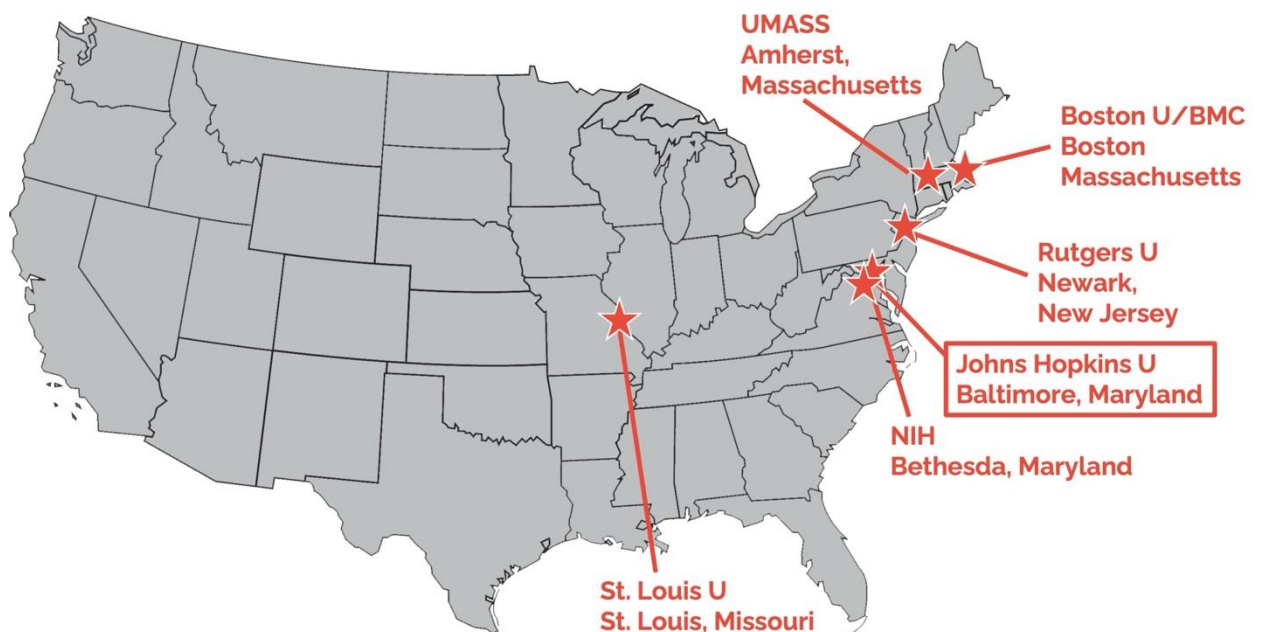
Both Indo-US governments have further supported the scientific research goals of RePORT India by expanding the number of sites represented across the country, especially by involving scientists and participants from the Northern and North-eastern parts of the country. In addition to the existing group of TB patients and their household contacts across nine Indian sites in the RePORT India Phase II Common Protocol, the consortium plans to support the enrollment of 1500 adult and child patients who are suspected of having TB outside the lungs, 588 adult patients with TB inside the lungs, and 794 household contacts of adult patients with TB inside the lungs. On the following pages, the Phase II CRSs and their study focus areas are outlined.

RePORT India Phase 2



Central Biorepository: Department of Virology & Biotechnology, ICMR-NIRT

Data Coordination Center: JIPMER



Phase 2 Scientific Aims

AIM 1. DIAGNOSTICS

Evaluate Novel Diagnostics & Biomarkers of Diverse States of Mtb Infection

Participating Patient Cohort: Diagnostic (New TB suspects)
Leads: Dr. Sonali Sarkar (JIPMER) and Dr. Jerry Ellner (Rutgers)

Participating Patient Cohort: Cohort B (XDR HHCs)
Leads: Dr. Tester Ashavaid (Hinduja) and Dr. Jeff Tornheim (JHU)

AIM 2. MARKERS OF TREATMENT RESPONSE

Participating Patient Cohort: Cohort A (Active TB disease)

2.A: Identify TB Treatment Response Biomarkers
Leads: Dr. Vijay Viswanathan (MVDRC) and Dr. Hardy Kornfeld (UMass)

2.B: Investigate Host-Related Mechanisms of Treatment Failure
Leads: Dr. Vidya Mave (BJGMC-JHU CRS) and Dr. Natasha Hochberg (BMC)

2.C: Investigate Pathogen-related Mechanisms & Predictors of Recurrence
Lead: Dr. David Alland (Rutgers)

AIM 3. LUNG INJURY & IMPAIRMENT

Identify Markers of Lung Injury Associated with Unfavorable TB Treatment Outcomes

Participating Patient Cohort: Cohort A (Active TB disease)
Leads: Dr. DJ Christopher (CMC Vellore), Dr. Ashutosh Aggarwal (PGI Chandigarh), and Dr. Akshay Gupte (BU)

AIM 4. RESISTANCE TO INFECTION

Mechanisms of Protection against TB in Exposed Persons

Participating Patient Cohort: Cohort B (Phase I HHCs)

4.A: Examine Host Antimicrobial Pathways in Inducing their infection resistant (IR) Phenotype in HHC

4.B: Test if IR & Plasma Differ in Modulating Macrophage-Mediated Restriction of Mtb Growth & Evaluate AB Repertoires of Plasma from the IR and infection susceptible (IS) Cohorts

Leads: Dr. Padmini Salgame (Rutgers), Dr. Subash Babu (NIRT-ICER), and Dr. Kamakshi Prudhula Devalraju (BMMRC)

AIM 5. PROGRESSION TO DISEASE

Identify Immunologic Markers of Persons at Highest Risk of Progress of Latent TB Infection to TB

5.A: Stored Samples: Validation of PREDICT29 in Progressors & Nonprogressors from RePORT Sites
Participating Patient Cohort: Cohort B (Phase I HHCs)
Leads: Dr. Padmini Salgame (Rutgers) and Dr. Luke Elizabeth Hanna (NIRT)

5.B: Immune & Hormone Studies in Freshly Collected Samples
Participating Patient Cohort: Cohort B (Phase II HHCs)
Leads: Dr. Vijaya Valluri (BMMRC) and Dr. Ramakrishna Vankayalapati (SLU)

In addition to these five aims, we will assess cross-cutting epidemiologic and COVID-19 related aims.

Central Tuberculosis Biorepository



The Central Biorepository (CBR) is one of the most significant achievements of the RePORT India Consortium. It was established in 2016 at ICMR–National Institute for Research in Tuberculosis (ICMR-NIRT), Chennai, with funding support from the Department of Biotechnology, Govt. of India, and became fully operational in 2017 when Phase 1 of RePORT India Common Protocol was rolled out. Over the years, the CBR evolved into a state-of-the-art Biorepository and transitioned to its new location at the ICMR-NIRT's Tiruvallur campus. The CBR is equipped with high quality storage equipment fitted with real-time temperature monitoring probes, advanced HVAC infrastructure, secure access control systems, power back-up facilities, and other safety devices.

The CBR serves as the central archival facility for biospecimens collected from participants enrolled across nine Clinical Research Units (CRUs) throughout India, including individuals with active TB (Cohort A), household contacts of active TB cases (Cohort B), and presumptive TB participants (Diagnostic cohort). The repository currently stores a diverse range of biospecimens, including plasma, peripheral blood mononuclear cells (PBMCs), whole blood, PAXgene RNA samples, raw sputum, TRIzol-treated sputum, urine, saliva, stool, *Mycobacterium tuberculosis* isolates, and extrapulmonary TB specimens. A major strength of the CBR is its comprehensive quality management system.

Since the inception of RePORT India, the CBR has coordinated consortium-wide training programs for study coordinators, laboratory personnel, and data managers to ensure standardized implementation of the Common Protocol. ICMR-NIRT qualified as the in-country provider of the PBMC Cryopreservation Proficiency Testing Program and has been certified by the Immunology Quality Assurance (IQA) Program of Duke University, USA. Through ongoing quarterly external quality assessment surveys, the CBR oversees proficiency of participating laboratories of the Consortium in preparing PBMCs for long term storage. Continuous competency-based trainings, refresher programs, laboratory working group calls and laboratory support visits help the CBR maintain harmonized specimen processing and storage practices across the Consortium.



OVERVIEW



The repository operates under harmonized Standard Operating Procedures (SOPs), barcode-based specimen tracking through FreezerPRO®, and rigorous internal and external quality assurance programs. Periodic quality control assessments evaluate PBMC viability and recovery, DNA and RNA integrity, and recovery of stored *M. tuberculosis* cultures, ensuring the long-term suitability of archived specimens for advanced immunological, molecular, and translational research. All activities are conducted in accordance with Good Clinical Laboratory Practice (GCLP) guidelines and established biosafety, ethical, and data governance frameworks. The effectiveness of these systems has been demonstrated through two PPD audits of the Central Biorepository, both of which were completed without any major non-compliances, highlighting the CBR's commitment to maintaining the highest standards of quality and regulatory compliance.

To date, the CBR has archived approximately **222,000** biospecimen vials collected through various RePORT India studies, representing one of the largest TB-focused biorepository resources in India. In addition, nearly 7,000 biospecimen vials from specialised participant groups have been distributed to investigators for national and international collaborative research projects. These biospecimens have supported studies on TB diagnostics, biomarkers, host immune responses, treatment outcomes, metabolomics, genomics, and vaccine-related research, facilitating scientific discoveries and strengthening collaborative TB research efforts.

By providing a sustainable platform for high-quality biospecimen storage, quality assurance, and equitable access to well-characterized samples, the CBR continues to strengthen India's TB research and serves as a valuable national resource for advancing scientific discoveries aimed at TB prevention, diagnosis, treatment, and control.





Data Coordination Center

Vision

To advance tuberculosis research through collaborative, data-driven science by enabling high-quality data management, fostering innovation, and generating evidence that improves public health outcomes in India and globally.

Mission

- Strengthen multi-institutional partnerships for high-impact tuberculosis research.
- Facilitate secure data and biospecimen management and sharing across consortium sites.
- Support evidence-based research for TB prevention, diagnosis, treatment, and control.
- Integrate advanced data management technologies, quality systems, and analytical approaches to accelerate scientific discovery.

About

Since 2019, the Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER) has served as the Data Coordination Center (DCC) for RePORT India, building upon the foundation established during Phase I. The DCC serves as the digital and scientific, operational, and informatics backbone of the consortium, ensuring that high-quality clinical, epidemiological, laboratory, imaging, biospecimen, and multi-omics data generated across participating institutions are transformed into reliable, harmonized, secure, and analysis-ready research resources.

The DCC provides centralized coordination for all data-related activities, including study database development, electronic data capture systems, real-time monitoring, quality assurance, statistical support, data integration, secure storage, advanced analytics, regulatory compliance, and controlled data sharing. By integrating data generated across multiple clinical sites and laboratories, the DCC ensures standardized data collection, interoperability, reproducibility, and scientific rigor across all RePORT India studies.

A major strength of the DCC is its ability to integrate diverse data modalities generated during the natural history of TB. These include demographic and clinical information, radiological imaging, microbiology, immunology, transcriptomics, proteomics, metabolomics, lipidomics, genomics, host genetics, pharmacokinetics, digital biomarkers, environmental exposures, and longitudinal treatment outcomes. Rather than functioning as isolated datasets, these data streams are harmonized into a unified research ecosystem that supports systems biology investigations, biomarker discovery, predictive modelling, and precision public health.

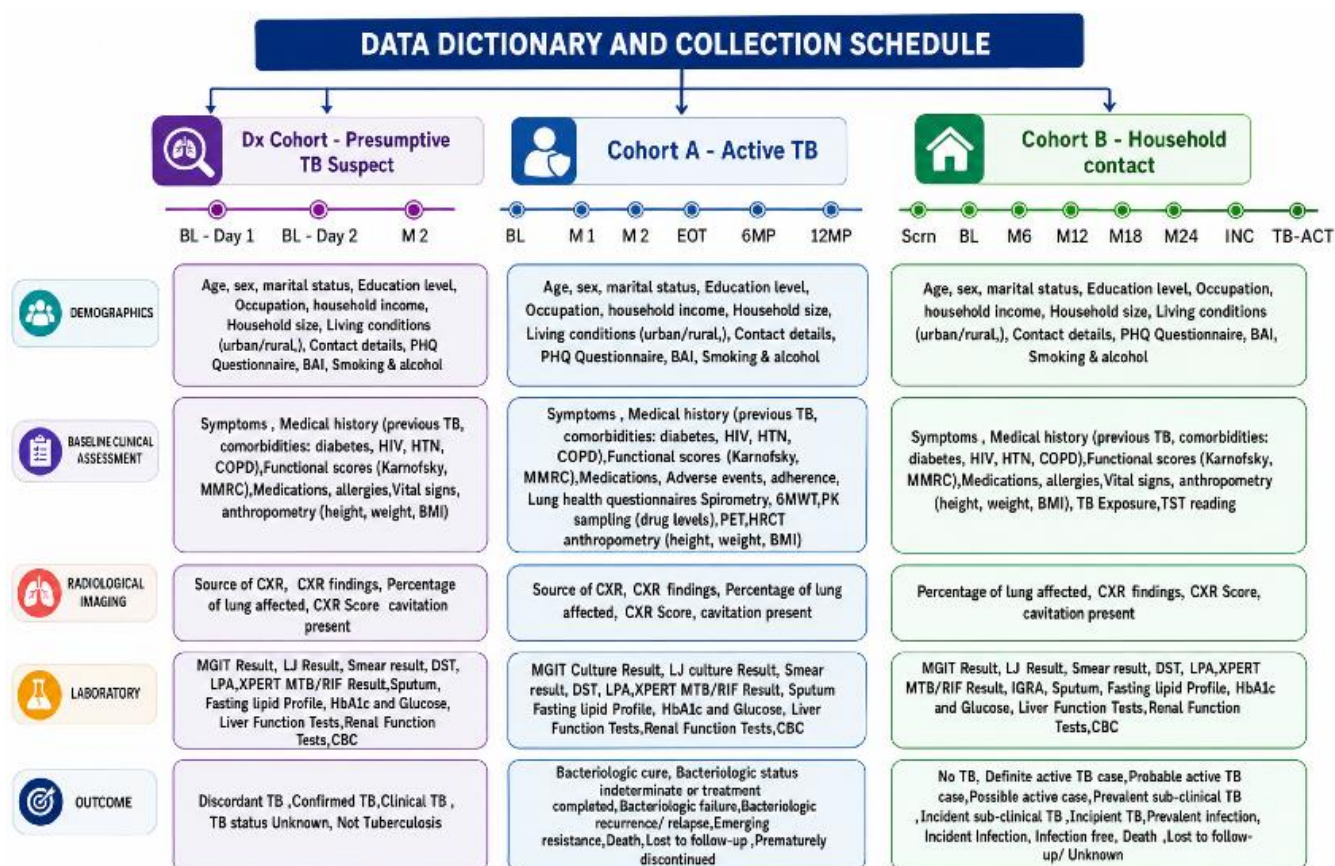
Our multidisciplinary team comprises Data Managers, Quality Control Managers, Data Analysts, Statisticians, Information Technology Specialists, and Technical Support personnel who collectively maintain robust systems that support high-quality, reproducible research.



Data Coordination Center

On-premises Infrastructure

REDCap and FreezerPro are hosted on dedicated on-premises physical servers at JIPMER, providing a secure, high-performance infrastructure for centralized clinical data capture and biospecimen management. The locally managed environment ensures data security, regulatory compliance, reliable system performance, routine backup, disaster recovery, and seamless support for multicentre RePORT India research activities.



Digital Infrastructure

The DCC utilizes internationally recognized platforms to support standardized data and biospecimen management.

REDCap

- Electronic Case Report Forms (eCRFs)
- Real-time data validation
- Query management
- Secure cloud and local server infrastructure

FreezerPro

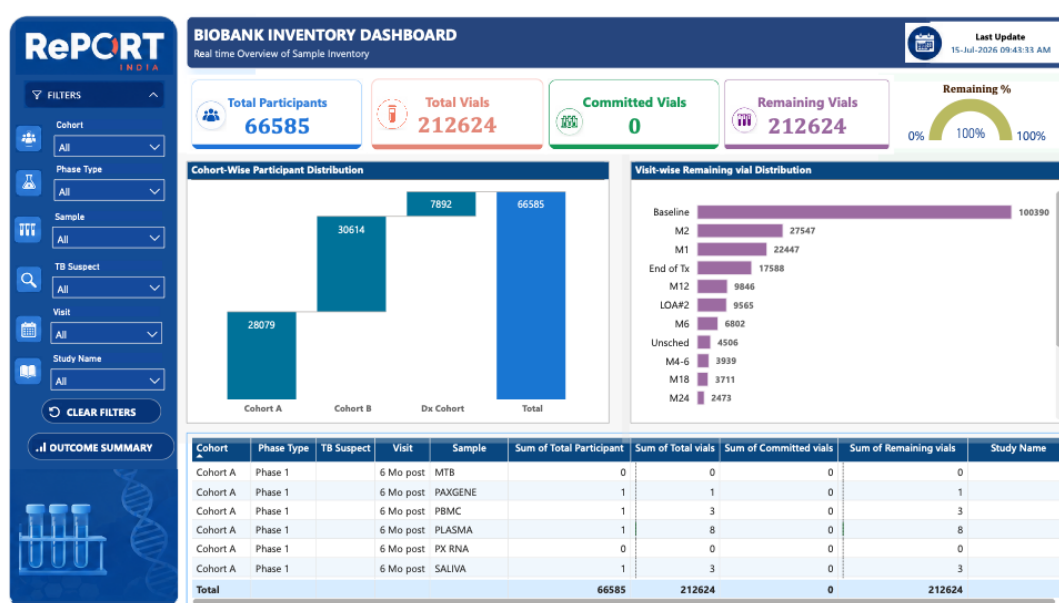
- Biospecimen inventory management
- Sample tracking across participating sites
- Barcode-enabled specimen traceability

Currently, the DCC manages harmonized data from nine clinical sites, generating regular quality assurance reports, monitoring study performance, and ensuring compliance with consortium protocols.

Data Coordination Center

Core Functions of the DCC

- Standardization of Case Report Forms (CRFs) and data dictionaries
 - Development and maintenance of REDCap databases
 - Extensive experience in using REDCap for web-based data capture in research studies.
- Key features include:
- Validated data capture with robust audit trails.
 - Automated data exports to statistical packages.
 - Integration with external data sources.
 - Centralized data validation and quality assurance
 - Biospecimen tracking using FreezerPro
 - Statistical and analytical support
 - Data harmonization across clinical sites aligns with global data
 - Regulatory compliance and data security
 - Performance monitoring through routine dashboards and reports



Data Management Capacity

The DCC has extensive expertise in designing and validating electronic databases compliant with 21 CFR Part 11 requirements. Rigorous User Acceptance Testing, standardized SOPs, and robust quality assurance procedures ensure reliable, secure, and reproducible data throughout the research lifecycle.

Capacity Building and Training

Building sustainable research capacity remains a key objective of the DCC.

Major initiatives include:

- Training investigators and study coordinators on REDCap and electronic data capture
- Capacity building in Good Clinical Practice (GCP) and Clinical Data Management
- Development of standardized data management workflows and quality assurance procedures
- Continuous technical support for consortium sites
- Adherence to 21 CFR Part 11

The Rutgers University Data and Operations Management Center (DOMC) has provided technical mentorship to JIPMER Data Hub, including training on REDCap, FreezerPro, RADAR dashboards, data management best practices, networking, archival strategies, disaster recovery, and quality management systems. A monitoring visit conducted by PPD recognized the DCC's strengths in secure infrastructure, redundant systems, audit trails, user training, and effective support for multicentre data collection.

Data Coordination Center

Looking Ahead

The RePORT India Data Coordination Center continues to strengthen the consortium's research ecosystem through innovation in digital health technologies, automated quality monitoring, advanced analytics, and secure data governance.

Future priorities include:

- Artificial intelligence-assisted data quality monitoring
- Machine learning-enabled predictive analytics
- Real-time research dashboards
- Integration of clinical, imaging, laboratory and multi-omics data
- FAIR data implementation
- Secure federated data sharing
- Strengthening collaborative research networks

Administration

RePORT India has established a collaborative governance structure composed of: 1) an Executive Committee led by two Chairs and two Co-chairs from India and the U.S.; 2) an Indo-U.S. Coordinating Hub; 3) three Scientific Working Groups (Basic Science, Clinical Epidemiology, Behavioral Science); 4) five Operational Working Groups (Common Protocol Leadership, Study Coordination, Publications Committee, Laboratory Management, and Data Management); and 5) a Data Coordinating Hub (JIPMER). The EC's mission is to set research priorities, guide scientific activities, and offer administration and logistics in support of research priorities.

The consortium is currently led by:

- Chairs: Dr. Sonali Sarkar (JIPMER, Clinical Epi) and Dr. Amita Gupta (JHU, Clinical Epi)
- Co-Chairs: Dr. Vijaya Valluri (BMMRC, Basic Science) and Dr. Padmini Salgame (Rutgers, Basic Science)

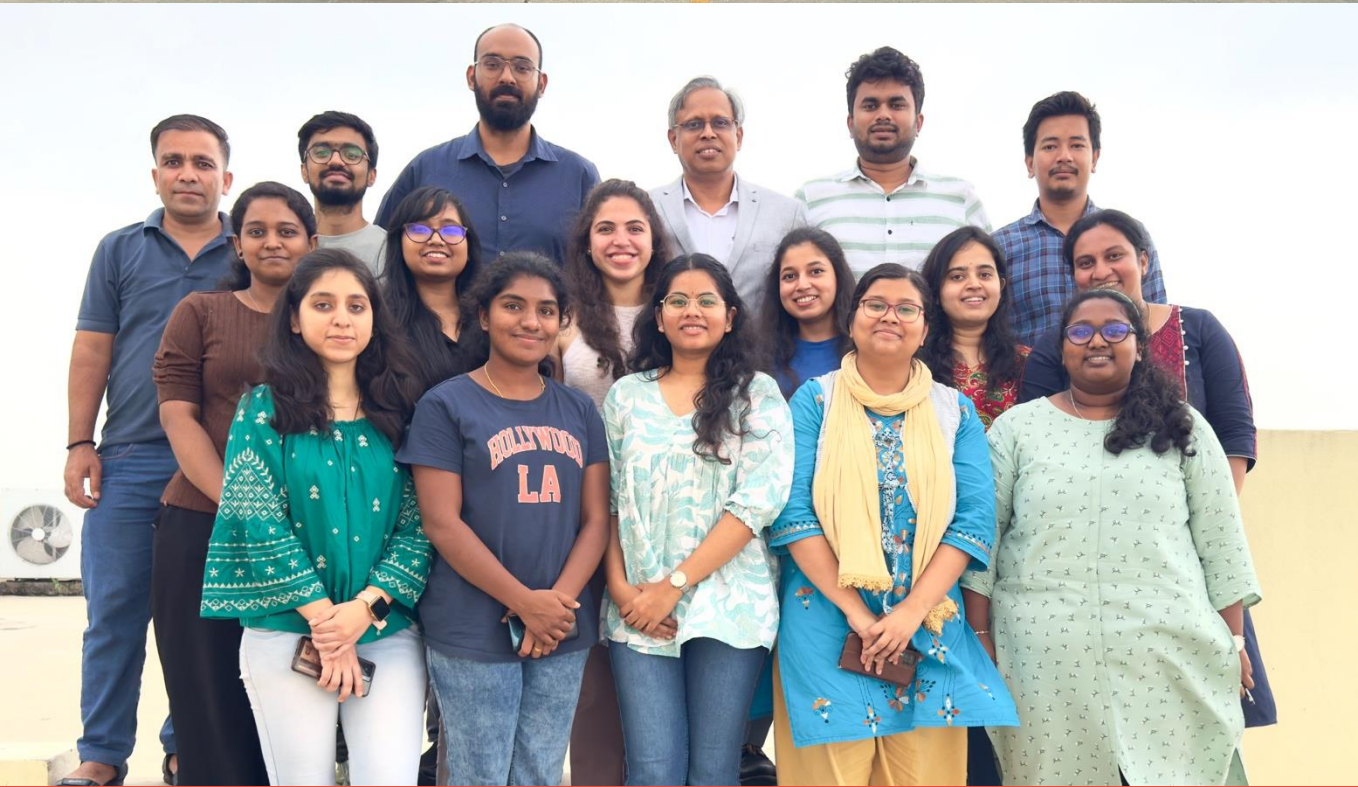
Funding

The RePORT India Consortium is supported with bilateral funding from the Government of India's (GOI) Department of Biotechnology (DBT) and the U.S. National Institutes of Health's (NIH) National Institute of Allergy and Infectious Diseases (NIAID), Division of AIDS (DAIDS), and Office of AIDS Research (OAR). CRDF Global administers and oversees the funding from the U.S. government.

RePCORT

INDIA

FUNDING



Funding in USD

India Institutions: CRDF Funding	\$2,873,543
US Institutions: CRDF Funding	\$6,394,563
India Institutions: DBT Funding	\$2,565,507
Total	\$11,833,613

Funding in INR

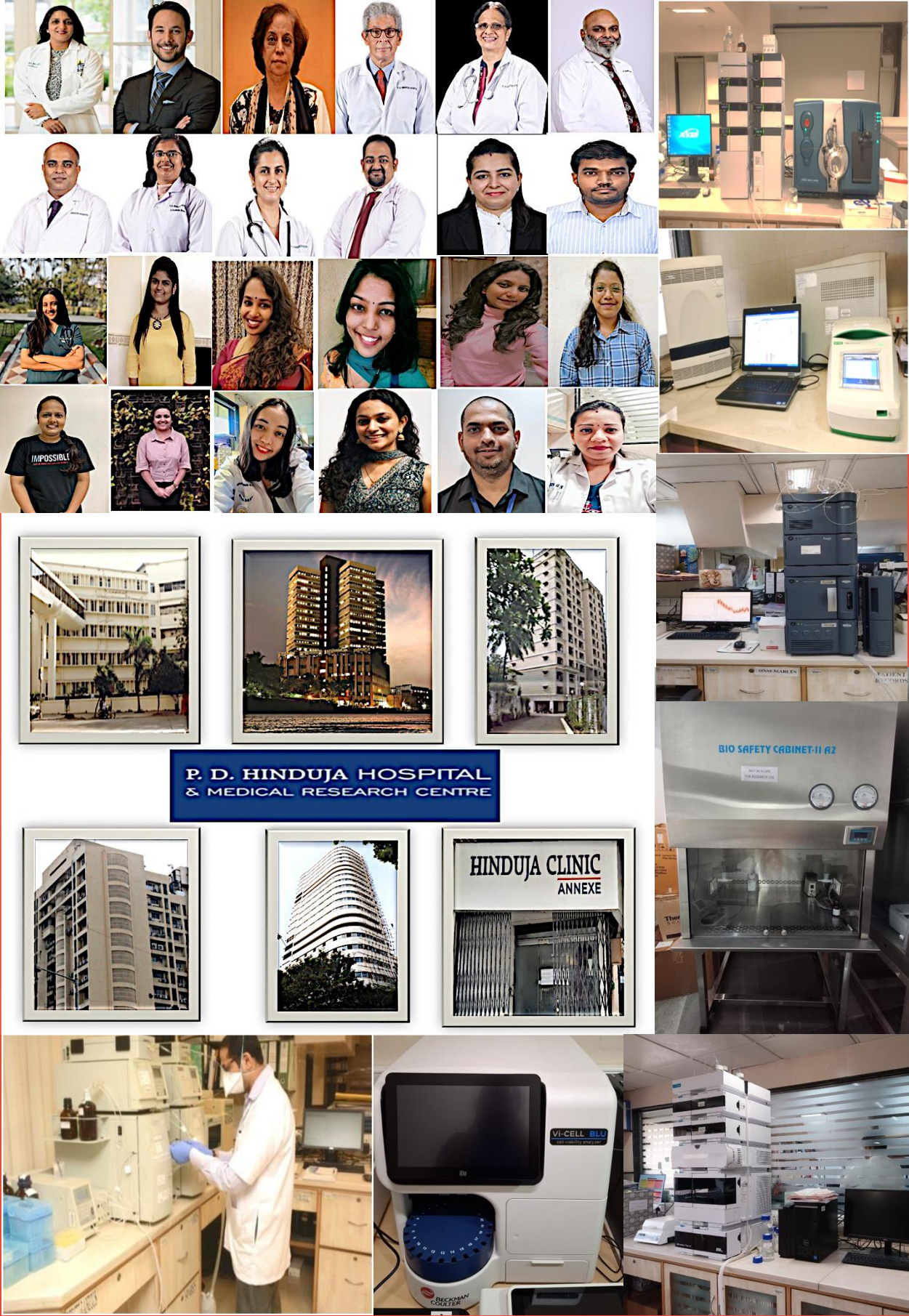
India Institutions: CRDF Funding	₹22,84,92,155
US Institutions: CRDF Funding	₹60,07,96,269
India Institutions: DBT Funding	₹21,80,68,073
Total	₹1,04,73,56,497

CMC Vellore





JUNIOR INVESTIGATOR ABSTRACTS



TITLE	INVESTIGATORS
GLI Race-Neutral versus Regional Spirometry Reference Equations for Classifying Post-Tuberculosis Lung Disease in India	Spurthi Kodali , Mandar Paradkar, Balamugesh Thangakunam, Sanjay Gaikwad, Bhavani PK, Ashutosh Aggarwal, Vidya Mave, Amita Gupta, Devasahayam J Christopher, Akshay N Gupte on behalf of the RePORT-India TB Research Consortium
Nutritional supplementation in malnourished individuals with latent M. tuberculosis infection is accompanied by host-microbiome interactions and its immune and metabolic correlates	A. VanValkenburg , K. Jain, V. Kaipilyawar, S. Lakshminarayanan, M. Dauphinais, P. Sinha, N. Rajkumari, P.B. Narasimhan, P. Salgame, W.E. Johnson
Characterization of Angiogenic Factors and Their Receptors in Active Pulmonary Tuberculosis Patients Stratified by Nutritional Status	Agalya Vanamudhu , Guruprashath Mohan, Vibash Kalyaan, Kailash Rajpurohit, Sivasubarmanian K, Syed Hissar, Shanmugam Sivakumar, Vijay Viswanathan, Hardy Kornfeld, Subash Babu, Nathella Pavan Kumar
Immune markers and cytokine profiles of adult and paediatric patients with Pulmonary and Extra Pulmonary Tuberculosis	Venkata Sanjeev Kumar Neela , Kamakshi Prudhula Devalraju, Vara Lakshmi Mallidi, Rajesh Kumar Radhakrishnan, Mohammad Soheb Ansari, Vinay Kumar Nandicoori, Ramakrishna Vankayalapati, Vijaya Lakshmi Valluri
Monocyte <i>TNF</i> -Superfamily Signaling Dysregulation in Tuberculosis–Type2 Diabetes Mellitus Comorbidity	Guruprashath Mohan , Nandita G, Rajeshkumar Radhakrishnan, Jai Priya GV, Kaviya Suresh, Syed Hissar, Ramakrishna Vankayalapati, Nathella Pavan Kumar

GLI Race-Neutral versus Regional Spirometry Reference Equations for Classifying Post-Tuberculosis Lung Disease in India

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Affiliated RePORT Team: India/US

Key Words: Post-Tuberculosis Lung Disease; Spirometry; Global Lung Function Initiative Race-Neutral Reference Equations; Indian Regional Reference Equations; Lung Function

Primary Category: Epidemiology

Background: Post-tuberculosis lung disease (PTLD) affects over half of individuals completing TB treatment. India contributes to one-third of the global burden, yet the optimal spirometry reference equation for classifying PTLD remains unclear. We compared Global Lung Function Initiative (GLI) race-neutral and Indian regional reference equations for classifying PTLD in adults with pulmonary TB in India.

Methods: We studied 103 adults (>18 years) with drug-sensitive PTB enrolled within 7 days of treatment initiation. Participants underwent pre- and post-bronchodilator spirometry per ATS/ERS standards, 6-minute walk testing (6MWT), and quality-of-life assessment using the St. George's Respiratory Questionnaire (SGRQ) at successful treatment completion. Associations of lung function z-scores and ventilatory defects (obstructive or restrictive), classified using GLI race-neutral equations and Indian regional equations, were examined in relation to SGRQ scores and 6MWT distance.

Results: GLI race-neutral equations classified more participants with ventilatory defects, particularly restrictive spirometry, than Indian regional equations (71.6% vs 61.8%, $p = 0.024$). Specifically, using GLI race-neutral equations, 3.9% had obstructive, 52.9% restrictive, and 14.7% mixed defects, compared to 7.8%, 44.1%, and 9.8%, respectively, using Indian regional equations; correspondingly, the proportion classified as normal was lower with GLI race-neutral equations (26.8% vs 37.9%, $p = 0.01$).

Continued: GLI Race-Neutral versus Regional Spirometry Reference Equations for Classifying Post-Tuberculosis Lung Disease in India

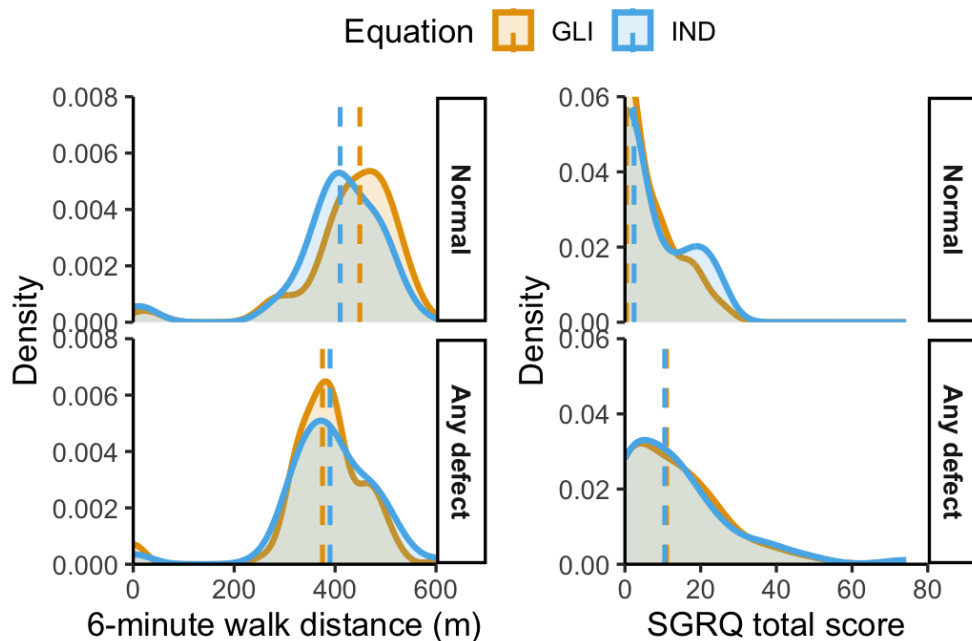
GLI race-neutral equations-defined FEV₁ and FVC z-scores showed stronger correlations with SGRQ scores and 6MWT distance. GLI race-neutral equations-defined defects were associated with higher SGRQ scores (median 11.0 [IQR 1.6, 20.1] vs 0.4 [0.0, 9.2]; $p = 0.001$) and lower 6MWT distance (380 [340, 415] vs 449 [400, 490] m; $p = 0.005$); discrimination was weaker with Indian regional equations SGRQ (10.9 [1.6, 19.3] vs 2.6 [0.0, 15.0], $p = 0.079$) and 6MWT (390 [341, 452.8] vs 410 [375, 471.2] m, $p = 0.336$).

Conclusions: Among treated adult PTB cases in India, GLI-defined ventilatory defects and z-scores showed stronger associations with respiratory health and functional status than Indian equations.

Figure 1: Distribution of Functional and Quality-of-Life Outcomes by Ventilatory Defect Classification Using GLI and Indian Reference Equations

Distribution of 6MWT and SGRQ Scores by Ventilatory Defect
(GLI vs Indian Reference Equations)

Median = dashed line



Density plots show the distribution of 6-minute walk test (6MWT) distance and St. George's Respiratory Questionnaire (SGRQ) total scores stratified by ventilatory defect status (Normal vs Any defect). GLI = Global Lung Function Initiative (race-neutral equations); IND = Indian regional reference equations. Dashed lines indicate median values. Ventilatory defects include obstructive, restrictive, and mixed patterns.

Nutritional supplementation in malnourished individuals with latent M. tuberculosis infection is accompanied by host-microbiome interactions and its immune and metabolic correlates

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Affiliated RePORT Team: Rutgers University, JIPMER, Boston Medical Center

Key Words: TB, Nutrition, Immunity Response, Microbiome, Metabolism

Primary Category: Nutrition

Background: Undernutrition constitutes an important global risk factor for TB and previous studies have shown an increase in enrichment scores of TB risk signatures, yet the mechanisms linking nutritional status to immune dysfunction remain poorly characterized. To elucidate these relationships, our study employs microbiome profiling and whole-blood RNA sequencing in household contacts with latent TB infection to define how undernutrition shapes the host-microbiome landscape and whether nutritional supplementation can reverse the associated immune deficits.

Design/Methods: Paired stool microbiome and whole-blood bulk RNA-seq was performed on 260 samples from 145 LTBI individuals at two visits (V1, baseline; V6, follow-up) from a RePORT-India cohort. Subjects were malnourished (BMI<18.5; n=59 at V1) or well-nourished (n=84). Helminth status was also recorded for all individuals. Paired V6-vs-V1 microbiome profiling samples were analyzed using MetaScope and Animalcules in R, and pathway analysis using PICRUST. Differential expression was performed in baseline samples from malnourished individuals (n=54 paired), including a >4 kg weight-gain subgroup (n=12). Enrichment scores of TB Risk signatures and pathways were performed with the TBSignatureProfiler, METAFlex, KEGG, and the Human Cytokine Dictionary. Microbes and host genes/pathways were analyzed using canonical correlation analysis.

Results: Following the nutritional intervention, microbial composition shifted to less inflammatory profiles, while host pathways demonstrated decreased expression of microbe-related pathways, such as Tryptophan/IDO-kynurenine metabolism and oxidative phosphorylation. Furthermore, both the microbiome and overall gene expression patterns of the malnourished group showed a moderate shift toward the well-nourished group as determined by dimension reduction. Metabolic signature enrichment scores, cytokine enrichment, and TB Risk signature RISK4 scores also correlated with both changes in microbes and diet. IFN- γ pathway enrichment decreased in response to nutritional intervention.

Conclusions: Nutritional supplementation in malnourished LTBI individuals is associated with changes in microbe and gene expression patterns that are trending toward a well-nourished profile with regards to inflammatory microbial abundance. Enrichment signatures of Hallmark Immune, cytokine, and metabolism pathways coordinated with a decline in the blood interferon signature and its metabolic correlates (tryptophan/IDO, oxidative phosphorylation).

Characterization of Angiogenic Factors and Their Receptors in Active Pulmonary Tuberculosis Patients Stratified by Nutritional Status

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Key Words: Active Pulmonary Tuberculosis (PTB), Angiogenic Factors, Body Mass Index (BMI), Malnutrition, Metabolic Factors

Primary Category: Diagnostics & Laboratory

Background and Rationale: Pulmonary tuberculosis (PTB) is often associated with malnutrition, which may aggravate disease severity through immune and metabolic dysregulation. Angiogenic mediators, including Angiopoietins (Angio-1 and Angio-2), Angiopoietin-like proteins (AngioL-3 and AngioL-4), Vascular Endothelial Growth Factors (VEGF, VEGF-C and VEGF-D), and their receptors (VEGF-R1, VEGF-R2 and VEGF-R3), play key roles in inflammation, vascular remodeling, and lipid metabolism. However, the impact of nutritional status on the systemic regulation of these mediators in PTB remains unclear.

Methods: In this longitudinal study, circulating plasma levels of ten angiogenic and metabolic factors were quantified by ELISA in 88 adults with bacteriologically confirmed active PTB, recruited from ICMR-NIRT, Chennai (2015-2020). Participants were stratified by body mass index (BMI) into low BMI (LBMI, BMI <18.5 kg/m², n=44) and normal BMI (NBMI, BMI ≥18.5 kg/m², n=44) groups. Plasma levels were assessed at baseline (M0) and after six months of anti-tuberculosis therapy (M6) using the Mann-Whitney U test with Holm's correction and Spearman correlation analysis.

Results: At baseline, LBMI patients showed significantly elevated Angio-2, AngioL-3, AngioL-4, VEGF, VEGF-C, VEGF-R1, and VEGF-R3 compared to NBMI patients. Following ATB therapy, most mediators declined in both groups; however, AngioL-3, VEGF, VEGF-C, and VEGF-R1 remained persistently elevated in LBMI patients at M6, while VEGF-C paradoxically increased in the NBMI patients. Spearman correlation revealed divergent BMI-biomarker patterns between groups, with post-treatment NBMI patients exhibiting exclusively negative correlations.

Conclusions: These findings indicate persistent angiogenic dysregulation in undernourished PTB patients, highlighting links between malnutrition, angiogenesis, and TB pathogenesis. Integrated treatment strategies combining antimicrobial therapy with targeted nutritional rehabilitation and host-directed interventions are essential to restore vascular homeostasis and improve long-term outcomes.

Immune markers and cytokine profiles of adult and paediatric patients with Pulmonary and Extra Pulmonary Tuberculosis

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Affiliated RePORT Team: RePORT Hyderabad Site (BMMRC & CCBM)

Key Words: Pediatric Tuberculosis, Pulmonary Tuberculosis (PTB), Extra-pulmonary Tuberculosis (EPTB), Cytokine Profiles, Immunophenotyping, DHEA (Dehydroepiandrosterone)

Primary Category: Basic Science

Background and Rationale: The clinical presentation of *Mycobacterium tuberculosis* (*Mtb*) infection varies significantly with age. Children below 15 years of age are more susceptible to *Mtb* infection compared to adults due to immature immune system. While adults predominantly develop pulmonary form (PTB), children are distinctively prone to disseminative extra-pulmonary TB (EPTB), driven by biological mechanisms that remain unclear. Effective host defence requires a coordinated interplay between cellular immunity, systemic nutrition and endocrine signalling. However, the exact immunometabolic and hormonal differences that distinguish adult responses from pediatric vulnerability are not well defined. Comparing cell phenotypes, hormone levels, and antigen-specific cytokine responses across adult and pediatric PTB and EPTB patients is essential to understand the specific immune defects that allow *Mtb* to disseminate in young patients.

Methods: Patients were diagnosed and categorised into pulmonary and extra pulmonary tuberculosis following NTEP guidelines. A total of 197 TB patients were enrolled under four categories: PTB adults (N=80), EPTB adults (N=45), PTB children (N=35), and EPTB children (N=37). Blood was collected from all the treatment naïve patients after obtaining informed consent. From the freshly isolated PBMCs, we determined various immune cell populations, (NK, monocyte and T-cell sub populations including T-regulatory cells) using flow cytometry. A part of the PBMC (2 x 10⁶ cells) were cultured with γ irradiated *M. tuberculosis* (H37RV) (10 μ g/mL) and ESAT-6 + CFP-10 antigens (10 μ g/mL) using standardized protocols. The culture supernatants were collected after 96 hours to measure cytokine and chemokine levels by ELISA. Hormones levels in the plasma were estimated by ELISA and the CBC counts from blood were determined by auto analyser.

Results: Pediatric patients (both PTB and EPTB) were uniformly underweight (BMI less than 18.5 kg/m²), showing significantly lower BMI values than adult PTB (p=0.0315) and EPTB (p=0.0312) counterparts. Children also displayed haematological changes, with significantly higher RBC counts (PTB: p=0.024; EPTB: p=0.032) and platelet counts (PTB: p=0.004; EPTB: p=0.005) than adult counterparts. Immunophenotyping of baseline PBMCs revealed a tapered

Continued: Immune markers and cytokine profiles of adult and paediatric patients with Pulmonary and Extra Pulmonary Tuberculosis

innate compartment in children, whose CD14⁺ cell percentages were significantly lower in both PTB ($p=0.012$) and EPTB ($p<0.0001$) groups compared to adults; pediatric EPTB cases uniquely demonstrated a reduction in CD4⁺CD25⁺FoxP3⁺ regulatory T cells ($p=0.019$). Following PBMC stimulation with ESAT-6 and CFP-10, pediatric PBMCs showed a polarized cytokine profile relative to adults, marked by significantly lower IL-1 β production (PTB: $p=0.009$; EPTB: $p=0.026$) but significantly elevated IL-6 levels (PTB: $p=0.0053$; EPTB: $p=0.049$). This childhood immune difference coincided with a systemic endocrine deficit, as plasma DHEA levels were significantly lower in children across both PTB ($p=0.01$) and EPTB ($p=0.003$) cohorts.

Conclusion: Anaemia is highly prevalent among TB patients, especially in specific demographic groups, those with abnormal hematological parameters, and significant radiological findings. Routine screening and management of anaemia could improve TB outcomes.

Recommendations: These findings define a specific immunometabolic and endocrine phenotype that distinguishes pediatric tuberculosis from adult disease. The combination of severe wasting (low BMI), haematological stress (elevated RBCs/platelets), and a skewed antigen-specific cytokine response (low IL-1 β , high IL-6) indicates an immature or exhausted defence system in children, may be driven by systemic lack of immunomodulatory DHEA support. Crucially, the simultaneous depletion of innate CD14⁺ monocytes and CD4⁺CD25⁺FoxP3⁺ regulatory T cells uniquely defines the pediatric EPTB profile. This dual failure in initial pathogen surveillance and inflammatory control provides a cellular basis explaining why younger patients are highly susceptible to extra-pulmonary bacterial dissemination. Further, mechanistic studies would pinpoint the defective markers and pathways responsible for extra-pulmonary bacterial dissemination in children.

Monocyte *TNF*-Superfamily Signalling Dysregulation in Tuberculosis – Type2 Diabetes Mellitus Comorbidity

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Affiliated RePORT Team: ICMR-National Institute for Research in Tuberculosis, Prof. M. Viswanathan Diabetes Research Center

Key Words: Tuberculosis, Diabetes Mellitus, TB-T2DM comorbidity, Monocytes, TNF Signalling, Cytokines

Primary Category: Diagnostics & Laboratory

Background and Rationale: Type 2 diabetes mellitus (T2DM) increases tuberculosis (TB) susceptibility two to three-fold and is associated with poor treatment outcomes, increased relapse and delayed pathogen clearance. Monocytes play a significant role in eliminating *Mycobacterium tuberculosis* (M.tb), where hyperglycaemia causes immune dysregulation in TB-T2DM comorbid individuals. TNF signalling pathways regulate macrophage activity and

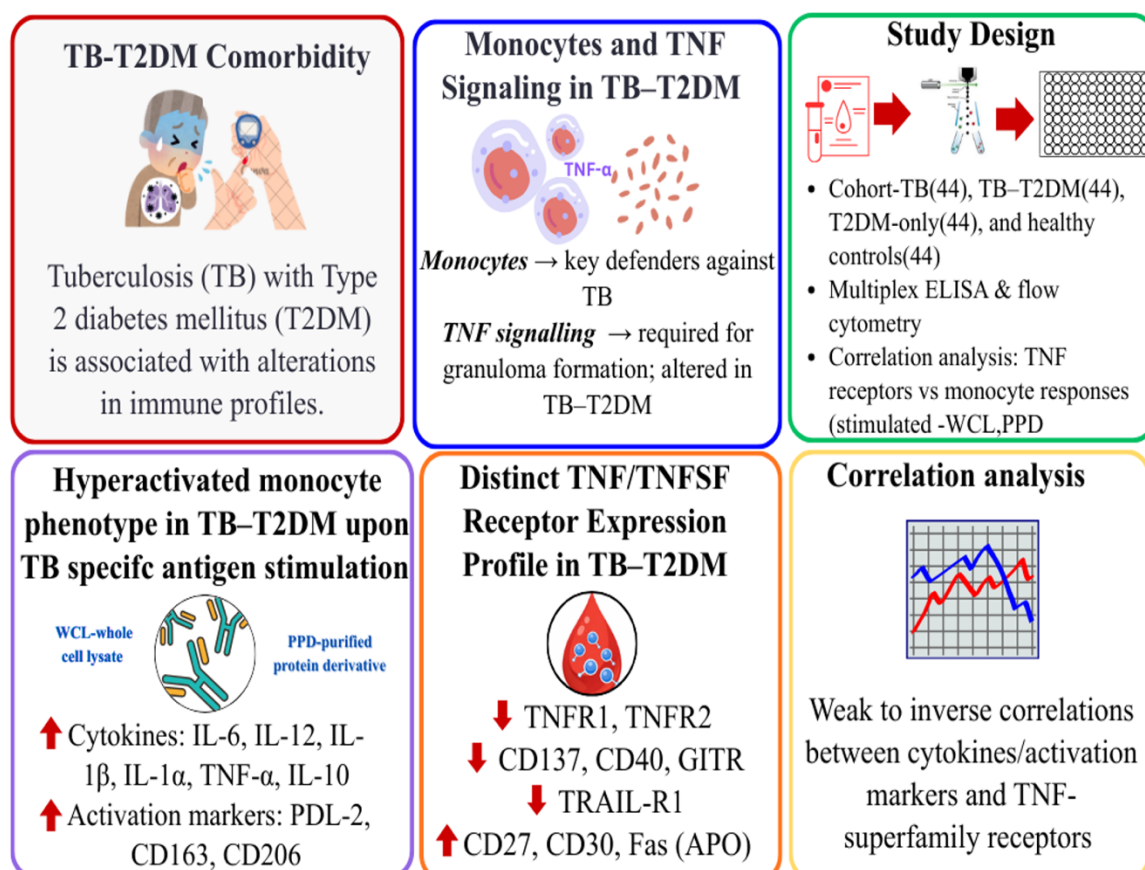
Monocyte TNF-Superfamily Signalling Dysregulation in Tuberculosis-Type2 Diabetes Mellitus Comorbidity

granuloma maintenance, and their dysregulation may contribute to disease severity. Although T2DM is known to alter monocyte subsets and promote hyper-inflammatory responses during TB, the mechanisms underlying dysregulated TNF-superfamily pathways in TB-T2DM comorbidity remain underexplored.

Methods: A cohort of 176 individuals (TB, TB-T2DM, T2DM-only and healthy controls) was evaluated. Classical monocytes (CD14⁺CD16⁻; n=20/group) were analysed by flow cytometry for intracellular cytokine-associated (IL-6, IL-12, IL-1 β , IL-1 α , TNF- α) and activation markers (PD-L1, PD-L2, CD80, CD86, CD163, CD206) upon stimulation with PPD, whole-cell lysate and TLR2/4 ligands. Plasma TNF-superfamily receptors and co-stimulatory molecules (n=44/group) were quantified by multiplex ELISA. Spearman correlation, protein-protein interaction (PPI), KEGG and Gene Ontology analyses were performed.

Results: TB-T2DM individuals showed significantly increased cytokine-associated markers (IL-6, IL-12, IL-1 β , IL-1 α , TNF- α , IL-10) and activation markers (PD-L2, CD163, CD206) upon antigen stimulation (p<0.05). Multiplex ELISA revealed decreased CD137, CD40, GITR, TNFR1/2, TRAIL-R1/R2 and increased CD27, CD30 and Fas expression in TB-T2DM (p<0.05). Correlation analysis showed weak-to-inverse associations between cytokine and activation markers across TNF receptor superfamily members. PPI analysis identified TNFRSF1A, TNFRSF9 and CD95 as central hubs, while KEGG enrichment highlighted NF- κ B, death-signalling and TNF receptor binding pathways.

Conclusion: Hyperglycaemia-associated monocyte dysfunction in TB-T2DM is linked to altered TNF-superfamily receptor expression and impaired immune regulation. These findings highlight the influence of hyperglycaemia in worsening immune function in TB-T2DM comorbidity, though further studies are required to establish biological and clinical relevance.





GRANTS & SUBSTUDIES



Screening camp at community



Screening



Clinical Assessment

Doctors examination

Chest Xray



Screening camp conducted at JIPMER OPD



RePORT International & CFAR Supplemental Funded Projects

TITLE	PARTNERS	CRDF #	START DATE	INVESTIGATORS
Metabolites, Inflammation, Type 2 Diabetes Mellitus and Tuberculosis Patients	ICMR-NIRT, Saint Louis U, De La Salle Medical & Health Sciences Institute	RICC	2025	Kumar NP, Radhakrishnan RK, Yu CY
Predictors of Resistance Emergence Evaluation in MDR-TB Patients	Hinduja, Fiotech, Boston U, Rutgers U, Vanderbilt U	RICC	2024	Arora PR, Ridolfi F, Gao Y, Horsburgh CJ, Rodrigues C, Rolla VC, Safi H, Sterling T, and the Hinduja-RePORT Brazil team
Metabolites, inflammation, T2DM and tuberculosis patients	ICMR, Saint Louis U, De La Salle Medical and Health Sciences Institute, Philippines, U of Texas	RICC	2024	Pavan Kumar N, Radhakrishnan RK, Yu C (RePORT Philippines), A. Aquino, K. Singh, R. Vankayalapati.
Evaluating the clinical utility of a novel RNA-based assay for predicting TB treatment outcomes and diagnosing paucibacillary TB	Weil Cornell, BJGMC, JHU, Makerere U, Oxford U	RICC	2024	Zainabadi K, Karyakarte R, Pradhan N, Gaikwad S, Paradkar M, Mave V, Gupta A, Joloba M, Nasinge E
Local Capacity Building to Develop Novel Drug-Resistant TB Testing and High-Throughput Multiplex Protein Measurement Programs in Pune, India	BJGMC	RICC	2023	Gupta A, Karyakarte R, Mave V, Pradhan N, Armstrong D
RePORT India Consortium Strengthening Equipment Funding	BJGMC, Hinduja	RICC	2023	Tornheim J, Udwadia Z, Ashavaid T, Rodrigues C, and the BJMC team
TB-RiCC Laboratory Enhancement and Capacity Building	JIPMER	RICC	2023	Sarkar S, Ellner J
IFNg-independent T cell-mediated protection in Mycobacterium tuberculosis infection	Rutgers, JIPMER, BJGMC, JHU	RICC	2023	Sarkar S, Joseph N, Salgame P
Innovative Modelling for Predicting TB Treatment Outcomes in Global Cohorts	JHU, FIOTEC, Vanderbilt U, RePORT India, RePORT Brazil	RICC	2022	Krishnan S, Robinson M, Andrade B, Sterling T, Gustavo, Gupta A, Gupte N, RePORT India, RePORT Brazil
Impact of Latent TB Infection and Trained Immunity on Susceptibility to SARS- CoV-2 Infection in India and the Philippines	Rutgers, JIPMER, U of Philippines Manila	RICC	2021	Salgame P, Sarkar S, Marissa AM (RePORT Philippines)

RePORT International & CFAR Supplemental Funded Projects

Continued

TITLE	PARTNERS	CRDF #	START DATE	INVESTIGATORS
Impact of Latent TB Infection and Trained Immunity on Susceptibility to SARS-CoV-2 Infection in India and the Philippines	Rutgers, JIPMER, U of Philippines Manila	RICC	2021	Salgame P, Sarkar S, Marissa AM (RePORT Philippines)
Associative BRICS Research in COVID-19 and Tuberculosis (ABRICOT)	FIOTEC, Wits Health Consortium, NIRT-ICER	RICC	2021	
T Cell Biomarkers and T-Regulatory Responses to Pediatric TB	Emory, JHU, BJGMC, NIRT	65373	2020	Rengarajan J, Kagal A, Kinikar A, Mave V, Padmapriyadarsini C, Hanna L, Paradkar M
Pregnancy Associated Immune Responses to TB and HIV in India and South Africa (PARTHISA study)	JHU, BJGMC, Wits Health Consortium, Cornell	65344	2020	Gupta A, Martinson N, Mathad J, Bhosale R, Kagal A, Alexander M, Kulkarni V
Pharmacokinetic Assessment of MDR-TB Drugs in the Treatment of TB Meningitis	JHU, PD Hinduja, Beijing Chest Hospital, BJG MC, Wits Health	65351	2020	Tornheim JA, Ashavaid T, Rodrigues C, Udwardia Z, Duan H, Sangle S, Varaiava E, Dooley K, Ignatius E, Mave V, Gupta A, Shivakumar SVBY, Chawla P, Patil S, Kulkarni V
Inflammasome Genetics and TB Treatment Outcomes	UPenn, JHU, UMass, BU, NIRT, MVDRC, BGJMC	65375	2020	Bisson G, Gupte A, Viswanathan V, Gupta A, Kornfeld H, Hanna L, Babu S, Andrade B, Dhanasekaran M
Host RNA Expression for Diagnosis and Monitoring of Pediatric TB in Africa and India	NIRT, BGJMC, JHU, Univ. Cape Town, Imperial College, London	64080	2019	Kinikar A, Paradkar M, Hissar S, Workman L, Dawre R, Gupte N, Tornheim JA, Kulkarni V
Determination of Efficacy of Xpert PCR Ultra And Transcriptional Signatures In The Diagnosis of Pleural Tuberculosis	CMC, Vellore G University of Cape Town, SA	64074	2018	Christopher DJ, Keertan D
Validation of Transcriptional Signature to Predict Active TB Disease among Advanced HIV Patients	RePORT Brazil, BMC, BJGMC, JHU, Rutgers	63158	2017	Mave V, Rolla V, Salgame P, Kadam D, Andrade B, Gupta A, Meshram S, Kulkarni V, Ellner J
Molecular Signatures of Tuberculosis- Diabetes Interaction (MSTD1) Study	JHU, UMass, BJGMC, NIRT, BU, MVDRC	63459	2017	Kornfeld H, P Chandrasekaran, Gupte A, Mave V, Bharadwaj R, Golub J, Andrade B, Paradkar M, Luke H, Kulkarni V, Gupte N, Shivakumar SVBY, Gupta A

Internal RePORT India Awards Made By NIH

TITLE	PARTNERS	START DATE	INVESTIGATORS
Building Respiratory Evidence for AI Tools and Health Equity (BREATHE)	CMC, U of Ibadan (Nigeria), U of Cape Town (South Africa)	2026	Christopher DJ, Balamugesh T, Gbadegsin FA, Esmail A, Zar H
Long term cardiac and pulmonary consequences of TB (LONG TB)	CMC, BU	2025	Christopher DJ, Balamugesh T, Gupte A
Biomarkers for TB Diagnosis and Treatment Response	BJGMC, NIRT, Emory, JHU	2016	Rengarajan J, Hanna LE, Mave V, Padmapriyadarsini C, Thiruvengadam K, Toidi A, Gupte N, Kulkarni V, Gupta A and CTRIUMPH team
Impact of HIV and Diabetes Mellitus on TB Drug Resistance and Recurrence	BJGMC, NIRT, JHU, MVDRC, UMass, Rutgers	2016	Mave V, Devi U, Padmapriyadarsini C, Mathema B, Vishwanathan V, Kornfeld H, Kreiswirth B, Golub J, Gupte N, Shivakumar SVBY, Gupta A
MDR-TB and HIV at RePORT Sites India	BJGMC, NIRT, JIPMER, JHU, BMC	2016	Horsburgh R, Padmapriyadarsini C, Mave V, Gupta A, Sarkar S
Validation and Fine Tuning of the Computer Aided Diagnosis of Pulmonary TB Model for the Indian Subcontinent	CMC	2016	Christopher DJ, Thangakunam B, Lal B, Agrawal A
Extracranial Involvement as Detected by Positron Emission Tomography Scan in Patients with Tubercular Meningitis	CMC	2016	Thangakunam B, Christopher DJ
Inflammatory Biomarkers as a Triage Test for Screening Symptomatic TB	JIPMER, Rutgers, BMC	2016	Ellner J, Salgame P, Sarkar S, Pleskunas J
Characterization of Monocyte Responses in Pulmonary TB Patients with or without Type 2 Diabetes	NIRT-NIH – ICER, MVDRC	2016	Kumar P

Internal RePORT India Awards Made By NIH

Continued

TITLE	PARTNERS	START DATE	INVESTIGATORS
Effect of Malnutrition on Latent TB	Approved: JIPMER, Rutgers, BMC	2016	Hochberg NS, Negi VS, Mahalakshmy T, Johnson WE, Salgame P, Pleskunas J
Determining Barriers to TB Care	JIPMER, BMC/BU	2016	Sabin L, Sarkar S, Hochberg NS, Fernandes P, Pleskunas J, Amsaveni
TH17 Cell Subsets as Potential Risk Markers of Latency and Active TB Infection in Household Contacts	BMMRC, SLU	2016	Devalraju KP, Neela VSK, Valluri VL, Vankayalapati K
Comparison of Available Purified- Protein Derivative (PPD) Tuberculin Skin Test (TST) Antigen Solutions in Detecting Latent Tuberculosis Infection in India	CMC, BJGMC, JIPMER, BMMRC, NIRT, JHU, BMC	2015	Christopher DJ, Shankar D, Roy G, Sarkar S, Prakash Babu S, Gupta A, Deluca A, Cox SR, Hochberg NS, Horsburgh R

Grants Awarded

GRANT TITLE	PARTNERS	GRANT SOURCE	START DATE
Interleukin-6 signaling, lung injury and post-TB lung disease in TB/HIV (AIRMAIL)	CMC, BJGMC, BU, JHU	NIH R01	2024
Nutritional Interventions to End Tuberculosis among persons with HIV in India (NUTRIENT-India)	BU, JIPMER	NIH K01	2023
Baseline pRescription According to Direct from Sputum Sequencing and TArgeted drug Concentration Strategy	Hinduja, JHU, UCT, UCSD, Vanderbilt	NIH R01	2023
Multiplexed Detection of Cell- free M. Tuberculosis DNA and Its Drug-resistant Variants in Blood	Hinduja, JHU, Tulane	NIH R01	2023
InTGS: Whole Genome Sequencing of MTB Clinical Strains for Determining Drug Resistance and Strain lineage in India: A Structured Nationwide approach	JIPMER, NII, ICGB, CCMB, NIBMG, BMMRC, BJGMC, PGI, Hinduja, NIRT	DBT, India	2023
Learning Effect of Parasites and Reinforcing Diets on TB (TB-LEOPARD)	JIPMER, BU	Burroughs-Wellcome Fund	2022
Childhood 'Omics' and Mycobacterium tuberculosis- derived BIOSignatures (COMBO) for TB Diagnosis	UCSF, BJGMC, JHU	NIH R01	2021
A Nanopore Biosensor for Leveling MTB Antigens in Blood	Tulane, JHU, BJGMC	NIH R01	2021
Rapid Research for Diagnostics Development in TB Network	CMC Vellore, UCSF	NIH/NIAID R01	2021
Innate Immune Response of LTBI+HIV+ Children	BMMRC, SLU	NIH/NIAID R01	2021
Learning about Experience with Nutritional Supplementation in Tuberculosis (LENS): An Exploratory Study	JIPMER, BU	Boston University of India (Seed Grant)	2021
Understanding Mycobacterium tuberculosis Mediated Host Metabolomics in Pulmonary Tuberculosis: Correlation with Disease Severity and Treatment Course	JIPMER IISER, Pune	PEER Women in Science SEED Grants 2021: National Academies	2021
Hybrid Trial for Alcohol Reduction among People with TB and HIV in India (HATHI)	BJGMC, JHU, London School of Hygiene and Medicine, DY Patil	NIH NIAAA R01	2020

Grants Awarded *Continued*

GRANT TITLE	PARTNERS	GRANT SOURCE	START DATE
VITAL TB (Vitamins And Latency in Tuberculosis)	JIPMER, BU	U.S. Department of State's Partnership 2020 educational initiative	2020
Thyroxine (T4) Hormone Inhibits Expansion of Immunosuppressive CD4CD25 ⁺ Foxp3 ⁺ (Tregs) Cells (Administrative Supplement for current R01 "IFN- independent inhibition of MTB growth in human macrophages")	BMMRC, SLU	R01	2020
Host and Microbiome Transcriptional Profiling in the Upper Airways for TB Susceptibility	JIPMER	CTSI Pilot Grant, BU, US	2020
Immune Responses and Effect of Disulfiram on MTB Infected PBMCs as a Potential Host Directed Therapy	BJGMC, NIRT, JHU, THSTI	Funding from Translational Health Sciences and Technology (THSTI)	2019
Dried Plasma Spots as a Simple Sampling Strategy to Measure Rifampicin Concentration to Facilitate this Service In Resource Limited Settings	CMC	Internal fluid research grant	2019
Evaluation of Diagnostic Potential of Aptamer-based Assays for Pulmonary Tuberculosis: A Pilot Study	CMC	THSTI	2019
Tuberculosis: Learning the Impact of Nutrition (TB LION)	JIPMER, BMC, Rutgers, Tufts, NIRT	Warren Alpert Foundation	2018
Whole Genome Sequencing of Drug Resistant Tuberculosis in India: Genotype-Phenotype Correlation, Clinical Impact of Resistance, and Sequencing Directly from Sputum	Hinduja, JHU	NIH/NIAID K23	2018
Validating a Th17 Switch as a Novel Correlate of Protective Immunity to TB	NIRT, BJMC, IISc, Bangalore, JHU Emory, JHU	DBT/ IISc	2018
Characterization of Genomics and Metabolomics among Individuals (TB-GWAS)	BJGMC, JIPMER, BMMRC, NIRT, PHRU, McGill, Brazil	NIH/NIAID R01	2018
Prevalence of Latent Tuberculosis in Rheumatoid Arthritis and Ankylosing Spondylitis	CMC	Internal fluid research grant	2018

Grants Awarded *Continued*

GRANT TITLE	PARTNERS	GRANT SOURCE	START DATE
The Effect of Appropriate Anti Tuberculous Treatment on Recovery of Pulmonary and Pleural Tuberculosis and the Impact of Tuberculosis on Lung Function and Quality of Life in Newly Diagnosed Patients	CMC	Internal fluid research grant	2018
Validation of Indigenously Developed Technology (TruNat MTB) for Diagnosis of Extra-pulmonary Tuberculosis: Multi-centric Validation	CMC, Hinduja, NIRT, AIIMS	ICMR	2018
Multicenter Phase II/III Double-Blind, Randomized, Placebo Controlled Study to Evaluate the Efficacy and Safety of VPM1002 in the Prevention of TB Recurrence in Pulmonary TB Patients after Successful TB Treatment.	RePORT India Sites	Serum Institute of India	2017-2022
Predictors of Resistance Emergence Evaluation in MDR-TB Patients on Treatment - (PREEMPT)	JIPMER, NIRT, BJGMC, Brazil, Vanderbilt, Rutgers, CDC, JHU, BMC, Hinduja	NIH/NIAID: R01	2017
Transcriptomic and Metabolomic Analysis of Microbiologically Confirmed Pediatric Tuberculosis Patients and Uninfected Household Contacts	BJGMC, JHU	Ujala Foundation Wyncote Foundation BWI-CTU C-TRIUMPH	2017-2022
Therapeutic Outcomes with Second-Line Drug Exposures in a Cohort of South African and Indian Patients with Drug Resistant TB: A Pharmacokinetic-Pharmacodynamic Assessment	Hinduja, PHRU, JHU	DBT/South Africa MRC	2017
Association of Lipid Mediators of Inflammation with TB Treatment Outcomes	JHU, NIRT, BJGMC	CTRIUMPH and Gilead Foundation	2017
The Role of Innate Immunity in the Acquisition of Sterile Protection Against TB Infection	U Colorado, JHU, BJMC	NIH R21	2017
IFN- γ Independent Inhibition of MTB Growth in Human Macrophages	BMMRC, SLU	NIH/NIAID R01	2017

Grants Awarded *Continued*

GRANT TITLE	PARTNERS	GRANT SOURCE	START DATE
MDR-TB Free: Monitoring Adverse Effects, Utilizing Resources Optimally, Knowing Resistance Patterns, and Treatment Strategy (MDR TB – MUKT)	Hinduja, JHU	Hinduja	2017
The Role of Monocyte Subpopulation in HIV+LTB+ Individuals and Development of Active TB	BMMRC, SLU	NIH R21 Indo-US Vaccine Program, RePORT India Cohort	2016-2018
Measuring TB Drugs in Hair as a Tool to Monitor Adherence, Exposure and Response	BJGMC, NIRT, JHU	NIH/NIAID: R21	2016-2018
Role of Iron Deficiency in Resistance of Women of Child-Bearing Age to Tuberculosis	JIPMER, BMC	NIH	2016-2017
Studying T cell Memory Responses for Understanding Protective Immune Response in Tuberculosis (TB)	CMC, NIRT, Saint Louis U	American Society of Tropical Medicine and Hygiene/ Burroughs Wellcome Fund)	2016
Impact of Immune Changes of HIV and Stages of Pregnancy on TB (PRACHITI)	BJGMC, NIRT, JHU	NIH/NICHD R01	2015-2020
Impact of Pregnancy on Tuberculosis	JIPMER, BMC	NIH/NIAID R01	2015-2018
Residual Respiratory Impairment Following Pulmonary Tuberculosis: The Lung Health Sub-Study	BJGMC, NIRT, JHU	UJALA/ Gilead Foundation/ RePORT India	2015-2017
D4GDI-mediated Immune Responses in LTBI+HIV+ Individuals	BMMRC, SLU	NIH R21 Indo-US Vaccine Program, RePORT India	2015-2017
Understanding of Tuberculosis Infection and Preventive Therapy Among Skin- Test Positive Household Contacts of Tuberculosis Cases	BJGMC, NIRT, JHU	NIH CFAR Fogarty D43	2015
T-regs Mediated Immune Responses in LTBI+HIV+ Individuals	BMMRC, SLU	SLU	2015
Compare Drug Levels in Newly Diagnosed or Relapsed PTB/ EPTB Following Daily ATT vs DOTS Regimen	CMC	Internal fluid research grant	2015
Impact of Personal Exposure to Black Carbon on Pulmonary Tuberculosis Severity	JIPMER BMC	Potts Memorial Foundation	2014-2018
Yield of TB using GeneXpert (Xpert MTB-Rif) by Induced Sputum Compared to Standard Sputum Samples	CMC	Internal fluid research grant	2014

Childhood 'Omics' and Mycobacterium tuberculosis-derived BIOSignatures (COMBO) for TB Diagnosis

Principal Investigators	Population	Funding
Adithya Cattamanchi (UCSF)	BJGMC Pune site contributed stored samples (plasma, urine) of eligible pediatric participants enrolled in the CTRIUMPH, RICC Pediatric, and TB Elispot studies.	NIAID
Joel Ernst (UCSF)		
Devan Jagannath (UCSF)		
Aarti Kinikar (BJGMC)		
Vidya Mave (BJGMC-JHU CRS)		
Mandar Paradkar (BJGMC-JHU CRS)		

Design: We will utilize banked blood and urine specimens among children being evaluated for TB in India, Uganda, South Africa, The Gambia, and Peru. We will measure Mtb-specific proteins and host proteins, and metabolites in the discovery and initial validation set of banked samples from 150 children with Confirmed TB, 150 children with Unconfirmed TB, and 300 children with Unlikely TB per NIH consensus definitions with and without HIV infection.

Aims:

1. Quantify levels of known Mtb proteins using an Electrochemiluminescence (ECL)-based assay ultra-sensitive
2. Perform an untargeted, shotgun proteomic and metabolomic approach to identify host proteins and metabolites that can serve as biomarkers for detection of childhood TB
3. Derive and validate the diagnostic accuracy of Mtb and/or host biosignatures for childhood

Status:

- Plasma metabolomics manuscript published (Nellis et al, 2026, Scientific Reports)
- Multiomics manuscript combining plasma proteomics and metabolomics- published (Mousavian et al, 2026, Clinical Proteomics)
- Urinary MTB protein ECL-based assays - assays completed, analysis and manuscript preparation are ongoing

Publications:

- Nellis MM, Luiz J, Jaganath D, Mousavian Z, Nkereuwem E, Wambi P, Calderon R, Paradkar M, Castro R, Nerurkar R, Franke MF, Kinikar A, Wobudeya E, Zar HJ, Jones DP, Segal M, Sigal G, Swaney DL, Cattamanchi A, Ernst JD, Ziegler TR, Kampmann B, Collins JM; COMBO Study. Multicohort assessment of plasma metabolic signatures of tuberculosis disease in children: a retrospective cross-sectional study. Sci Rep. 2026 Jan 23;16(1):3283. doi: 10.1038/s41598-025-32679-3. PMID: 41577684; PMCID: PMC12835163.
- Mousavian Z, Segal MR, Calderon RI, Luiz J, Nkereuwem E, Wambi P, Paradkar M, Franke MF, Källénus G, Kampmann B, Kinikar A, Sigal GB, Sundling C, Swaney DL, Wobudeya E, Zar HJ, Collins JM, Cattamanchi A, Ernst JD, Jaganath D. A multi-omics study reveals pathway-level insights and predictive biomarkers in pediatric TB. Clin Proteomics. 2026 Jun 8. doi: 10.1186/s12014-026-09614-3. Epub ahead of print. PMID: 42260364.

Markers of Lung Impairment in HIV-TB Coinfected Indian Adults

Principal Investigators	Sites	Population	Funding
Akshay Gupte (BU) Amita Gupta (JHU) Sanjay Gaikwad (BJGMC) Rajesh Karyakarte (BJGMC)	BJGMC	1. Adults (>18 years) with drug-susceptible pulmonary TB and HIV co-infection (HIV-TB group). 2. Adults with drug-susceptible pulmonary TB without HIV co-infection (TB group).	TREAT Asia NIAID/amfAR DBT

Design: A retrospective cohort study of already collected clinical samples and data from the CTRIUMPH study at BJGMC. BJGMC, Pune, India

Aims:

1. We will compare the degree of lung impairment between HIV-TB and TB participants at the completion of TB therapy. Lung impairment will be measured by pre-and post-bronchodilator spirometry. The primary outcome will be z-score standardized FEV1 using the Global Lung Initiative (GLI) reference equations. Secondary outcomes will include z-score standardized FVC and FEV1/FVC ratio. We will use linear regression to compare the degree of lung impairment in TB cases with and without HIV, adjusting for potential confounders. With 15 HIV-TB and 30 TB participants, we will have 80% power at 5% significance level to detect a 4.5 or higher percentile difference in lung function parameters between the two groups.
2. We will compare concentrations of inflammatory and metabolomic markers between HIV-TB and TB participants during TB therapy. Marker concentrations will be measured at individual time-points.

Status: Study completed

Manuscript Under Review: Metabolomic markers of post-tuberculosis lung disease. Baidya A, Quiroz A, Paradkar M, Karyakarte R, Selvaraju S, Mave V, Andrade B, Kornfeld H, Gupta A, Gupte AN

Inflammasome Genetics and Tuberculosis Treatment Outcomes

Principal Investigators	Sites	Population	Funding
Gregory Bisson (UPenn) Amita Gupta (JHU) Akshay Gupte (BU) Luke Hanna (NIRT) Subash Babu (NIH-NIRT-ICER) Vijay Vishwanathan (MVDRC) Sanjay Gaikwad (BJGMC) Rajesh Karyakarte (BJGMC)	BJGMC NIRT MVDRC	Adults (>18 years) with drug-susceptible pulmonary TB enrolled in the CTRIUMPH or EDOTS studies.	RICC

Design: Retrospective case-cohort analysis of already collected clinical samples and data from the CTRIUMPH and EDOTS studies.

Aims:

1. To determine the association between single nucleotide polymorphisms (SNPs) in candidate genes related to inflammasomes and microbiologic treatment outcomes in adults being treated for drug-susceptible pulmonary TB.
2. To determine the association between SNPs in candidate genes related to inflammasomes and pulmonary involvement in adults who successfully complete treatment for a new diagnosis of drug-susceptible pulmonary TB.

Status: Indian data have been analyzed. The data are currently being combined with the Brazil dataset, and pooled analyses are underway.

Manuscript Under Review: Neutrophil-to-lymphocyte ratio and post-tuberculosis pulmonary function: a potential marker for reduced function. Dinh J, Paradkar M, Gaikwad S, PK Bhavani, Suryavanshi N, Gupte N, Kulkarni V, Pradhan N, Law A, Aggrawal A, Thangakunam B, Hanna LE, Mave V, Padmapriyadarsini C, Gupta A, Christopher DJ, Gupte AN.

Molecular Signatures of Tuberculosis-Diabetes Interaction (MSTDI) Study—Metabolomics

Principal Investigators	Sites	Population	Funding
Hardy Kornfeld (UMass)	NIRT	1. TB with DM (TBDM)	RICC
Amita Gupta (JHU)	BJGMC	2. TB without DM (TB)	
Akshay Gupte (BU)	MVDRC	3. DM without TB (DM)	
Rajesh Karyakarte (BJGMC)	RePORT Brazil	4. Healthy controls (HC)	
Padma Chandrasekaran (NIRT)			
Vidya Mave (BJGMC-JHU CRS)			
Bruno Andrade (RePORT Brazil)			

Design: We will conduct a retrospective cohort study using collected demographic and clinic data and archived whole blood samples in the CTRIUMPH study as well as a small cross-sectional study of MTB uninfected adults with DM.

Aims:

1. Compare baseline metabolomic signatures between newly diagnosed drug-sensitive PTB patients with and without DM.
2. Characterize and compare longitudinal change in metabolomic signatures in response to ATT between newly diagnosed drug-sensitive PTB patients with and without DM.

Status: Study completed

Publication: Nancy Pandiarajan A, Kumar NP, Moideen K, Thiruvengadam K, Hissar S, Sivakumar S, Bethunaickan R, Viswanathan V, Kornfeld H, Babu S. Association of Altered Baseline Hematological Parameters with Adverse Tuberculosis Treatment Outcomes. *Pathogens*. 2025 Feb 4;14(2):146. doi: 10.3390/pathogens14020146. PMID: 40005523; PMCID: PMC11857862.

Immune Responses & Effect of Disulfiram on MTB Infected PBMCs: Disulfiram as a Potential Host Directed Therapy

Principal Investigators	Sites	Population	Funding
Amit Singhal (Singapore Immunology Network, Agency for Science, Technology and Research [A*STAR]) Ramandeep Singh (NCR Biotech Science Cluster) Rajesh Karyakarte (BJGMC) Amita Gupta (JHU) Padmapriyadarsini Chandrasekaran (NIRT) Vidya Mave (BJGMC-JHU CRS)	NIRT BJGMC	1. Adult PTB patients on TB treatment with an AUDIT score 8 (n = Up to 20) 2. Adult PTB patients on TB treatment with an AUDIT score < 8 (n = Up to 40) 3. Adult healthy contacts (n=Up to 20)	DBT, NIH

Design: We will conduct a cross-sectional study using already collected CTRIUMPh and RePORT India common protocol data (baseline demographic, clinical) and archived whole blood PBMC samples from the baseline visit to assess those with and without harmful use of alcohol as assessed by AUDIT scores 2-8. immunophenotyping will be performed by flow cytometry. Additional plasma cytokine and chemokine will also be considered.

Aims:

1. To assess immune responses among adult PTB patients with harmful alcohol use defined by an AUDIT score ≥ 8 compared to those with AUDIT scores < 8 at the time of treatment initiation.
2. Aim 2: To assess the effects of disulfiram on Mtb growth in PBMCs of alcoholic and nonalcoholic individuals

Status: Study discontinued

Evaluation of a Urinary Biomarker Assay for Diagnosis and Test of Cure for Tuberculosis

Principal Investigators	Population	Funding
Jeffrey Tornheim (JHU) Sanjay Gaikwad (BJGMC) Rajesh Karyakarte (BJGMC) Aarti Kinikar (BJGMC) Vidya Mave (BJGMC-JHU CRS)	Stored samples	NIH CFAR

Design: We will conduct a case-control diagnostic study nested within the CTRIUMPh cohort study using stored urine samples to identify positive results by the urine FujiLAM, conventional LAM, and the LAM and ESAT-6 nanocage assays. Samples have been collected from patients at multiple time points during treatment, and we will evaluate samples at enrollment (start of treatment), 2 months into treatment, and at the end of treatment (6 months).

Aims:

1. To assess the ability of the FujiLAM kit and a urine lipoarabinomannan glycan (LAM) nanocage assay and a urine ESAT-6 nanocage assay to diagnose tuberculosis (TB) among Indian adults and children with HIV and CD4 counts >100 as well as among age-matched Indian TB patients without HIV,
2. To compare the TB treatment response as measured by urine LAM and ESAT-6 nanocage assays to TB treatment response as measured by sputum conversion, radiographic improvement, and clinical improvement among Indian TB patients with HIV and CD4 counts >100 as well as among age-matched Indian TB patients without HIV.
3. (Exploratory): To assess the ability of FujiLAM kits and urine LAM and ESAT-6 nanocage assays to diagnose pediatric TB in Indian children with confirmed and unconfirmed TB.

Status: Study completed

Biomarkers for Tuberculosis Diagnosis and Treatment Response

Principal Investigator	Sites	Population	Funding
Jyothi Rengarajan (Emory)	NIRT BJGMC JHU Emory	Stored samples of participants enrolled in the Active TB cohort and Household contact cohort in the CTRIUMPh study	RePORT India

Design: Cross-sectional longitudinal study

Aims:

1. To evaluate biomarker performance on PBMCs from confirmed pulmonary TB and difficult-to-diagnose cases such as sputum smear-negative and HIV-infected individuals, extrapulmonary and pediatric TB patients.
2. To assess the ability of our biomarkers to monitor treatment response by selecting PBMCs from a subset of adult ATB patients, obtained at Time 0 (pre-treatment) and 1, 2, 6, and 12 after treatment initiation.
3. To use comprehensive immune profiling by mass cytometry (CyTOF) and multiparameter flow cytometry on a subset of ATB and control samples, to generate antigen-specific signatures of Adult TB, with the goal of discovering new markers that could further increase the sensitivity of our candidate biomarkers, particularly for difficult-to-diagnose TB cases.

Status: Study discontinued due to the non-viability of PBMCs

T-Cell Biomarkers and T-Regulatory Responses to Pediatric TB

Principal Investigators	Sites	Population	Funding
Jyothi Rengarajan (Emory) Vidya Mave (BJGMC-JHU CRS) Anju Kagal (BJGMC) Aarti Kinikar (BJGMC)	BJGMC	Stored samples of participants enrolled in the CTRIUMPh Pediatric Active TB cohort and RICC Pediatric study.	RICC

Design: We will use cryopreserved PBMC samples from CTRIUMPH cohorts: pediatric unconfirmed TB, confirmed TB, latent TB and no TB controls. We will also be leveraging the data and specimens from the RePORT International Coordinating Centre (RICC) Pediatric Diagnostic Cohort study at BJGMC, Pune and analyze PBMCs isolated from pediatric TB suspects.

Aims

1. Validate host T cell biomarkers for diagnosis of pediatric TB
2. Investigate the phenotype and functions of T-regulatory cells in pediatric TB

Status: Manuscript preparation underway, to be completed and submitted to journal in quarter 2 of year 2026.

A Nanopore Biosensor for Leveling MTB Antigens in Blood

Principal Investigators	Sites	Population	Funding
Tony Ye Hu (Tulane U) Robert Bollinger (JHU) Amita Gupta (JHU) Rajesh Karyakarte (BJGMC)	BJGMC Tulane U JHU	The purpose of the CTRIUMPH study was to evaluate the risk factors for TB among adults and children < 15 in India. Three cohorts were established: 1. Active TB cohort included adults with newly diagnosed active pulmonary TB (PTB) and children with TB 2. Household contacts cohort enrolling household members of active TB cases Stored plasma samples from participants enrolled in these three cohorts at the Pune site will be utilized for the proposed study for assessment and the performance of the portable prototype system of the protein-based nanopore technology to quantify Mtb target peptides. These CTRIUMPH samples, as well as their linked clinical and microbiological data, will be analyzed to evaluate the performance of the peptide detection assay.	NIH R01

Design: This ROI will employ components of our current platform in a study to develop and optimize a robust and portable protein nanopore-based platform (QuantiPep) that meets WHO guidelines for new TB diagnostics and which can sensitively detect Mtb antigens in adult and pediatric blood samples.

Shifting the assay from a mass spectrometry- to a nanopore-based system will allow rapid, sensitive and cost-effective TB detection and management in leaner clinical environments worldwide. Single channel recording technology is sensitive, specific, fast and affordable alternative to mass spectrometry. Nanopore ion currents are very sensitive to target molecule interactions as they occupy and translocate through the pore, and such interactions can generate signatures (current-time relationships) that are characteristic for a given target.

- Aims:**
1. Develop a sensitive and specific QuantiPep TB assay suitable for resource-limited settings:
 2. Validate Mtb antigen-derived peptides for TB diagnosis in a well-characterized cohort of adults and children with serially collected clinical, radiological and bacteriological data.
 3. Evaluate how serum levels of Mtb antigens change in adult PTB cases in during anti-TB therapy.

- Status:**
- The sample shipment for additional calibration and validation was shipped to Tulane lab for the assays.
 - Two laboratory scientists from our site were identified and travelled to Tulane lab in May 2025 to get trained on the nanopore study assay under the capacity building component. Further testing of validation cohort blinded samples is underway.
 - The original Principal Investigator (PI) for this project at Tulane (Dr. Tony Hu) has left the university for another institution. Tulane has officially requested that another Tulane investigator (Dr. Christopher Lyon) be appointed as the new PI and the NIH has recently approved this request.
 - Dr. Lyon has been a key scientific investigator for this project from the onset and is well positioned and experienced to be the PI. We do not anticipate any significant change in the scientific aims of this project and will be completing the laboratory work and subsequent research analyses with Dr. Lyon and the team at Tulane.

Identification of Biomarkers that Can Predict Progression from Latent TB Infection to Active TB Disease

Principal Investigators	Sites	Population	Funding
Subash Babu (NIH-NIRT-ICER)	NIRT	Adult and child household	ICMR
Rajesh Karyakarte (BJGMC)	BJGMC	contacts of adult PTB cases from	DBT
Vidya Mave (BJGMC-JHU)	NIH-	India enrolled in CTRIUMPh study:	NIH
CRS) Luke Hanna (NIRT)	NIRT-	1. HHCs of adult PTB cases, who	
Padmapriyadarsini	ICER	progressed to active TB	
Chandrasekaran (NIRT)		disease	
Amita Gupta (JHU)		2. HHCs of adult PTB cases, who did	
		not progress to active TB disease	

Design: Case-control analysis of stored specimens and associated data between progressors and non- progressors

Aims:

1. To identify soluble cytokine/chemokine biomarkers in antigen-stimulated QFT supernatants that can predict risk of progression to active TB disease

Publication: Daniel EA, Thiruvengadam K, Rajamanickam A, Chandrasekaran P, Pattabiraman S, Bhanu B, Sivaprakasam A, Paradkar M, Kulkarni V, Karyakarte R, Shivakumar SVBY, Mave V, Gupta A, Babu S, Hanna LE. QuantiFERON Supernatant-Based Host Biomarkers Predicting Progression to Active Tuberculosis Disease Among Household Contacts of Tuberculosis Patients. Clin Infect Dis. 2023 May 24;76(10):1802-1813. doi: 10.1093/cid/ciac979. PMID: 36582115.

2. To identify predictive miRNA biomarkers in QFT supernatants for risk of progression to active infectious TB

Publication: Daniel EA, Thiruvengadam K, Chandrasekaran P, Hilda N, Umadhankar P, Prashanthi P, Selvachithiram M, Pattabiraman S, Bhanu B, Sivaprakasam A, Paradkar M, Kulkarni V, Karyakarte R, Shivakumar SVBY, Mave V, Gupta A, Hanna LE. Discovery of a blood-based miRNA signature that can predict onset of active tuberculosis among household contacts of TB patients. Front. Tuberc. 2024 Oct 29; 2:1. doi:10.3389/ftubr.2024.1415346.

3. To identify small metabolite biomarkers in QFT supernatants for predicting risk of progression to active TB disease

Publication: Daniel EA, Upadhyay S, Selvachithiram M, Pattabiraman S, Bhanu B, Sivaprakasam A, Kulkarni V, Karyakarte R, Gaikwad S, Paradkar M, Yogendra Shivakumar SVB, Mave V, Gupta A, Prasad K, Hanna LE. Predictive metabolite signatures for risk of progression to active TB from QuantiFERON supernatants of household contacts of TB patients. Emerg Microbes Infect. 2025 Dec;14(1):2437242. doi: 10.1080/22221751.2024.2437242. Epub 2024 Dec 22. PMID: 39628384.

4. To analyze the plasma biomarker profile of HHCs who progressed to active TB and see if the profile reflected the pattern seen in QFT supernatants

Publication: Rajamanickam A, Ann Daniel E, Dasan B, Thiruvengadam K, Chandrasekaran P, Gaikwad S, Pattabiraman S, Bhanu B, Sivaprakasam A, Kulkarni V, Karyakarte R, Paradkar M, Shivakumar SVBY, Mave V, Gupta A, Hanna LE, Babu S. Plasma Immune Biomarkers Predictive of Progression to Active Tuberculosis in Household Contacts of TB Patients. J Infect Dis. 2024 Jul 19;jiae365. doi: 10.1093/infdis/jiae365. Epub ahead of print. PMID: 39028003.

Status: Study completed; four papers published; preparation of additional manuscripts underway

Host RNA Expression for Diagnosis & Monitoring of Pediatric TB in Africa & India RICC Pediatric Transcriptomic Study

Principal Investigators	Sites	Population	Funding
Lesley Workman (U of Cape Town)	Cape Town	Baseline samples from 365 South African children will be tested as part of the existing Levin biomarker validation study and are not budgeted here. Follow up samples from a subset of 200 South African children will be included as part of the proposed study.	RICC
Aarti Kinikar (BJGMC)	BJGMC		
Mandar Paradkar (BJGMC-JHU CRS)	NIRT		
Syed Hissar (NIRT)			
Michael Levine (Imperial College)			

Design: This study involves the collaboration of two RePORT consortia, South Africa and India, both high burden TB and TB-HIV settings with well-established pediatric cohorts of children with TB disease, together with the Imperial College group leading the current NIH-supported pediatric TB biomarker validation study.

Aims:

1. Primary Objectives: To derive and validate a global RNA expression signature for the diagnosis of pulmonary TB, and extra-pulmonary TB in children; and to identify longitudinal changes in RNA expression with TB treatment in children who have microbiologically confirmed or clinically diagnosed TB, using bio-banked samples from the South Africa and Indian cohorts and clinical information from the TB RePORT Common Protocol (CP) and India parent protocol databases.
2. Secondary Objectives: To establish a biorepository of samples that can be used for future pediatric TB diagnostic and pathogenesis studies.

Status: Interim analysis was completed earlier, Additional pediatric diagnostic cohort samples are identified for validation of the initial results. Planning of validation assays is yet to be completed in discussion with Imperial College team.

Residual Respiratory Impairment Following Pulmonary Tuberculosis: The Lung Health Sub-Study

Principal Investigators	Sites	Population	Funding
Rahul Lokhande (BJGMC) Shashikala Sangale (BJGMC) Sriram Selvaraju (NIRT) Akshay Gupte (BU) Amita Gupta (JHU)	BJGMC NIRT	1. Active TB cohort comprising 400 new adult pulmonary TB (PTB) cases. 2. Reference cohort comprising 400 adults without TB. 3. Cohort of 200 adults with chronic obstructive pulmonary disease (COPD) Each study site will enroll approximately 50% of the total sample size. COPD controls will be enrolled at BJGMC only.	NIAID

Design: Prospective cohort study nested within the CTRIUMPH study.

Aims:

1. To characterize trends in respiratory impairment among new adult PTB cases undergoing anti-tuberculous treatment (ATT) in India.
2. To identify host factors measured during the first 2 months of ATT initiation that are associated with respiratory impairment at ATT completion among new adult PTB cases in India.
3. To explore the impact of TB disease; alone and in combination with smoking exposure, indoor air pollution (IAP) exposure, HIV infection and diabetes mellitus (DM); on respiratory impairment up to 42 months following ATT completion among successfully treated adult PTB cases in India.
4. Characterize the chronicity and progression of lung impairment, and its responsiveness to bronchodilator therapy, in successfully treated PTB cases

Status: Study completed

Manuscript Under Review: The impact of undernutrition on post-tuberculosis lung disease: magnitude and mechanisms. P. Sinha, M. Karoly, S. Gaikwad, L.E. Hanna, Paradkar M, Gupte N, Kulkarni V, Pradhan N, Dauphinais M, Zhang V, Mave V, A. Gupta, Padmapriyadarsini C, Gupte AN.

Characterization of Genomics and Metabolomics among Individuals Highly Exposed, but Resistant to Mtb Infection (TB-GWAS)

Investigators	Sites	Population	Funding
Neel Gandhi (Emory)	BJGMC	Household contacts of adult	NIH R01
Yan Sun (Emory)	JIPMER	pulmonary TB cases from	
Sanjay Gaikwad (BJGMC)	BMMRC	parent protocols study, RePORT	
Rajesh Karyakarte (BJGMC)		India Common Protocol phase I	
Amita Gupta (JHU)		at all sites; and Prospective TB	
Vidya Mave (BJGMC-JHU CRS)		GWAS study enrollments at	
Neil Martinson (Perinatal HIV		BJGMC, Pune site.	
Research Unit, SA)			
Timothy Sterling (Vanderbilt, US)			
Bruno Andrade (Fiotec, Brazil)			

Aims:

1. To characterize a phenotype for resistance to Mtb infection using TST and IGRA results among household contacts recently exposed to TB.
2. To determine genetic predictors for resistance to Mtb infection.
3. To identify metabolomic markers associated with resistance to Mtb infection.

Status: Study completed

Abstract:

Gyorfy MF, Gandhi NR, Hui Q, Andrade B, Martinson N, Paradkar M, Prakash S, Devalraju KP, Figueiredo MC, Cordeiro-Santos M, Mofokeng NJ, Willis F, Sterling T, Gupta A, Sun YV on behalf of the TB GWAS collaboration. Genome-Wide Meta-Analysis Identifies Genetic Associations with Resistance to Mtb Infection. [poster presentation at 2025 Conference on Retroviruses and Opportunistic Infections, San Francisco 2025]

Preprint: Gandhi NR, Fernandes Gyorfy M, Paradkar M, Jennet Mofokeng N, Figueiredo MC, Prakash S, Prudhula Devalraju K, Hui Q, Willis F, Mave V, Andrade BB, Moloantoa T, Kumar Neela VS, Campbell A, Liu C, Young A, Cordeiro-Dos-Santos M, Gaikwad S, Karyakarte R, Rolla VC, Kritski AL, Collins JM, Shah NS, Brust JCM, Valluri VL, Sarkar S, Sterling TR, Martinson NA, Gupta A, Sun YV. Novel Genetic Locus Associated with Resistance to M. tuberculosis Infection: A Multi-Ancestry Genome-Wide Association Study. medRxiv [Preprint]. 2026 Mar 7:2026.03.06.26347614. doi: 10.64898/2026.03.06.26347614. PMID: 41867181; PMCID: PMC13004093.

Proteomic Discovery of Protein-based TB Recurrence and Death Signatures (IIT-M Proteomics Study)

Principal Investigators	Funding
Sanjeeva Srivastava (IIT-Bombay)	DBT
Sonia Krishnan (JHU)	NIH
Amita Gupta (JHU)	Phase 2
Mandar Paradkar (BJGMC-JHU CRS)	
Sanjay Gaikwad (BJGMC)	
Rajesh Kayakarte (BJGMC)	
Vandana Kulkarni (BJGMC-JHU CRS)	

Aims: To identify markers of TB recurrence/death by mass spectrometry

Status: Abstract accepted to the Journal of the American Society for Mass Spectrometry

Submitted Manuscripts: Plasma Proteomic Signatures Distinguish Treatment Resolution and Recurrence in Tuberculosis Patients- iScience

The Role of Innate Immunity in the Acquisition of Sterile Protection Against TB Infection

Principal Investigators

Adriana Weinberg (University of Colorado)

Vandana Kulkarni (BJGMC-JHU CRS)

Rajesh Kayakarte (BJGMC)

Funding

NIH R21

Design: To identify potential targets for new TB vaccines by characterizing the immune responses that distinguish individuals with sterilizing protection against TB (TB-resisters), defined by presence of TB-specific immune responses and absence of latent infection, from individuals with latent TB infection (LTBI-participants)

Status: Study closed

Publication: Jalbert E, Liu C, Mave V, Lang N, Kagal A, Valvi C, Paradkar M, Gupte N, Lokhande R, Bharadwaj R, Kulkarni V, Gupta A, Weinberg A. Comparative immune responses to Mycobacterium tuberculosis in people with latent infection or sterilizing protection. iScience. 2023 Jul 20;26(8):107425. doi: 10.1016/j.isci.2023.107425. PMID: 37564701; PMCID: PMC10410524.

Epidemiologic Factors Associated with TB Treatment Outcomes across RePORT International Consortia

Principal Investigators

Bruno Andrade (RePORT Brazil)

Timothy Sterling (RePORT Brazil)

Mark Hatherill (RePORT South Africa)

Thomas Scriba (RePORT South Africa)

Amita Gupta (RePORT India)

Sonali Sarkar (RePORT India)

Retna Mustika Indah (RePORT Indonesia)

Muhammad Karyana (RePORT Indonesia)

Yuhong Liu (RePORT China)

Jingtao Gao (RePORT China)

Marrissa Alejandria (RePORT Philippines)

Ray (Sang Nae) Cho (RePORT Philippines)

Funding

RICC

Design: Analysis of data collected from a prospective multi-site cohort study to determine the Impact of key non-communicable and communicable diseases on tuberculosis treatment outcomes and recurrence using data from multiple RePORT International consortia

Aims:

1. To create a harmonized analytical dataset from multiple RePORT International consortium sites
2. To determine the Impact of non-communicable diseases, including prediabetes and diabetes mellitus, and communicable diseases, including HIV, on tuberculosis treatment outcomes and recurrence, both globally and regionally

Status: Study Completed

Manuscript Under Review: Determinants of Tuberculosis Treatment Failure, Loss to Follow-up, Recurrence, and Death: A Multi-national Observational Cohort Study. Amorim G, Matreja P, Pentakota SR, Duda S, Ellner J, Figueiredo MC, Kim S, Alejandria MM, Malabad JCM, Cenal NL, Burhan E, Karyana M, Indah RM, Leslie A, Dheda K, Fourie B, Walzl G, Hatherill M, Gaikwad S, Christopher DJ, Sarkar S, Viswanathan V, Mave V, Gupta A, Kornfeld H, Cordeiro M, Mello F, Andrade B, Rolla VC, van der Heijden YF, Sterling TR, for the RePORT-International Consortium

Validation of Transcriptional Signature to Predict Active TB Disease among Advanced HIV Patients

Principal Investigators

Vandana Kulkarni (BJGMC-JHU CRS)

Funding

RICC

Design: The 1:1 case-control study to assess the performance of the 15 gene signature to detect TB among patients with advanced HIV. The cases would be advanced HIV patients (CD4 <100 cells/ul) with confirmed active TB and controls would be advanced HIV patients without any clinical and microbiologic evidence for active TB. The study was performed at BJGMC, Pune, India, Rio de Janeiro and Manaus at Brazil.

Study Exploratory Objectives: To assess and compare changes in the T cell activation of HLA-DR+ and CD38+ T cell subsets, cytokine profiles of inflammatory markers and co-relate blood transcriptional and cytokine signatures of TB among advanced HIV patients with or without TB.

1. To conduct testing and validation of the 15-gene signature to predict active TB disease among advanced HIV patients with CD4 <100 cells/ul.
2. To assess and compare the cytokine/chemokine signature that may be predictive for active TB among advanced TB-HIV and HIV patients in India and Brazil.

Status: Study completed; paper published

Manuscript Under Review: Immune Activation Profile Associated with Pulmonary Tuberculosis and Mortality Among Adults with Advanced HIV in India. Kulkarni V, Queiroz ATL, Karyakarte R, Deshpande P, Kante S, Pradhan N, Gupta A, Ellner J, Rolla VC, Gupte N Bollinger RC, Andrade BB, Salgame P, Nawani N, Mave V on behalf of the RePORT India TB Research Consortium

Publication: Kulkarni V, Queiroz ATL, Sangle S, Kagal A, Salvi S, Gupta A, Ellner J, Kadam D, Rolla VC, Andrade BB, Salgame P, Mave V. A Two-Gene Signature for Tuberculosis Diagnosis in Persons With Advanced HIV. Front Immunol. 2021 Feb 22;12:631165. doi: 10.3389/fimmu.2021.631165. PMID: 33692804; PMCID: PMC7937880.

Impact of Latent TB Infection and Trained Immunity on Susceptibility to SARS-CoV- 2 Infection in India and the Philippines

Principal Investigators

Padmini Salgame

Sonali Sarkar

Alejandro Marcelo

Marissa

Sites

JIPMER

University of

Philippines

Population

HHCs of pulmonary TB patients from

RePORT India Phase I studies; Index

COVID cases and their HHCs

(Philippines)

Funding

RICC

Design: About 300 household contacts of pulmonary TB patients enrolled through RePORT Phase 1 studies will be re-consented and stratified into 4 groups based on the presence of LTBI +/- and SARSCoV +/- . About 300 SARS-CoV-2 positive patients identified from the hospital database (index cases) and an additional 250 of their household contacts will be enrolled in Philippines. For each of the 4 groups, 20 subjects will be selected and the trained immunity of their monocytes and NK cells will be examined.

Aims:

1. Examine whether there is a correlation between LTBI and SARS-CoV-2 IgG seroconversion and/or COVID-19 disease severity
 - In India, determine the seroprevalence of COVID-19 in healthy household contacts of prior active PTB cases stratified according to the presence of LTBI
 - In the Philippines, determine the prevalence of LTBI in patients with confirmed COVID-19 infection and in their household contacts; and the association of LTBI with disease severity
2. Examine in a subset if enhanced trained immunity in LTBI positively correlates with protection from SARS-CoV-2 infection

Status: Enrollment and follow up completed. Study closeout activities are ongoing; sample processing is ongoing to perform bulk RNA sequencing to analyse gene expression CoV-2 study cohorts from PBMCs. And cytokine profiling is planned to compare trained immunity signatures and inflammatory profiles between pre- and post-COVID samples.

Therapeutic Outcomes with Second Line Drug Exposures in a Cohort of Patients with Drug Resistant TB: A Pharmacokinetic-Pharmacodynamic Assessment

Principal Investigators	Sites	Population	Funding
Tester F. Ashavaid (Hinduja)	Hinduja (India)	Cohort A: Adults and	SA MRC DBT
Camilla S. Rodrigues (Hinduja)	PHRU (South	adolescents ≥ 15 years of	Hinduja
Neil Martinson (PHRU, SA)	Africa)	age with MDR-TB (n=200)	Foundation
Ebbrahim Variava (PHRU, SA)			

Design: The study is designed to study the pharmacokinetic (PK) and pharmacodynamics (PD) profiles of second line TB drugs and develop PK-PD models to help understand efficacy of these drugs.

Aims:

1. To determine the pharmacokinetic parameters of second-line agents in South African and Indian patients receiving DR-TB treatment regimens with particular attention to moxifloxacin, linezolid, clofazimine, bedaquiline and SLI (Kanamycin, Amikacin)
2. To assess the MIC of these drugs using Thermoscientific Fisher Sensititre panels.
3. To characterize the population pharmacokinetics of these drugs in the study population and determine factors associated with low drug exposures
4. To study the association between drug exposures of second-line TB drugs and therapeutic outcomes in a pharmacokinetic-pharmacodynamic analysis among patients with DR-TB

Status: Data analysis ongoing

Publication: Resendiz-Galvan JE, Arora PR, Abdelwahab MT, Udwadia ZF, Rodrigues C, Gupta A, Denti P, Ashavaid TF, Tornheim JA. Pharmacokinetic analysis of linezolid for multidrug resistant tuberculosis at a tertiary care centre in Mumbai, India. *Front Pharmacol.* 2023 Jan 4;13:1081123. doi: 10.3389/fphar.2022.1081123. eCollection 2022. PMID: 36686664

Publication: Lokhande RV, Arora PR, Joubert A, Bhagure GR, Udwadia ZF, Gupta A, Rodrigues C, Tornheim JA, Wiesner L, Ashavaid TF; MDR-TB MUKT and RePORT India Study Team; Indo-South Africa Study Team. Quantitation of Plasma Bedaquiline Concentrations in Indian MDR-TB Patients Using Liquid Chromatography-Tandem Mass Spectrometry. *Biomed Chromatogr.* 2025 Dec;39(12):e70243. doi: 10.1002/bmc.70243. PMID: 41235782

Publication: Resendiz-Galvan JE, Arora PR, Lokhande RV, Udwadia ZF, Rodrigues C, Gupta A, Tornheim JA, Denti P, Ashavaid TF; The MDR-TB MUKT and Indo-South Africa Study Teams; MDR-TB MUKT and Indo-South Africa Study Teams. Evaluation of cycloserine dose regimens in an Indian cohort with multidrug-resistant tuberculosis: a population pharmacokinetic analysis. *Antimicrob Agents Chemother.* 2025 Oct;69(10):e0010125. doi: 10.1128/aac.00101-25. Epub 2025 Sep 2. PMID: 40891988

Manuscript Submitted: Lokhande RV, Arora PR, Bhagure GR, Joubert A, Udwadia ZF, Rodrigues C, Gupta A, Mave V, Raichur P, Gaikwad S, Khan R, Pradeep A, Wiesner L, Tornheim JA, Horsburgh CR, Ashavaid TF for the MDR-TB MUKT and RePORT India Team, Indo-South Africa Study Team and PREEMPT Study Teams. Analytical method development and validation for clofazimine in human plasma and application of LC-MS/MS based methods for clofazimine and bedaquiline in Indian MDRTB patients stratified by HIV coinfection.

Manuscript Submitted: Nkuhairwe IN, Arora PR, Lokhande RV, Resendiz-Galvan JE, Yadav P, Verma R, Wiesner L, Keny B, Udwadia ZF, Rodrigues C, Denti P, Tornheim JA, Wasmann RE, Ashavaid TF for the MDR-TB MUKT and Indo-South Africa Study Teams. Model-based evaluation of amikacin and ethambutol dosing strategies in Indian patients with multidrug-resistant tuberculosis.

Manuscript Drafted: Pharmacokinetics of moxifloxacin in an Indian population with multidrug-resistant tuberculosis.

CONTINUED: Therapeutic Outcomes with Second Line Drug Exposures in a Cohort of Patients with Drug Resistant TB: A Pharmacokinetic-Pharmacodynamic Assessment

Abstracts:

- Evaluation of cycloserine dose regimens in multidrug-resistant tuberculosis participants from India, presented at the Union World Conference on Lung Health, Bali, Indonesia, November 2024
- Population pharmacokinetics of moxifloxacin in Indian patients with multidrug-resistance tuberculosis, ACBICON Chandigarh, India, December 2024

MDR-TB Free: Monitoring Adverse Effects, Utilizing Resources Optimally, Knowing Resistance Patterns, and Treatment Strategy (MDR TB MUKT)

Principal Investigators	Sites	Population	Funding
Zarir F. Udwadia (Hinduja) Camilla S. Rodrigues (Hinduja) Tester F. Ashavaid (Hinduja) Amita Gupta (JHU) Jeffrey Tornheim (JHU)	Hinduja	1. Cohort A: Adults and adolescents ≥15 years of age with MDR-TB (n=200). 2. Cohort B: Adult and child household contacts of MDR-TB Cohort A participants with pulmonary TB (n=60).	Hinduja Foundation RePORT India NIH: K23

Design: This study comprises two prospective observational cohorts. Cohort A will enroll adults and adolescents ≥15 years with active multidrug resistant tuberculosis (MDR-TB). Cohort B will enroll adult & child household contacts of participants in Cohort A pulmonary MDR-TB cases.

Aims: To establish well-characterized prospective cohorts of active MDR-TB cases and their household contacts with associated biorepositories.

Cohort A Primary Objectives: To document participant outcomes including early treatment response, MDR-TB treatment-associated adverse events, mortality, and loss to follow-up.

Cohort B Primary Objectives: To assess rates of prevalent and incident TB infection and disease in household contacts of MDR-TB cases.

Cohort A Secondary Objectives

1. To evaluate the impact of comorbid diseases including diabetes mellitus, prediabetes, HIV, COPD, smoking status, alcoholism, depression, quality of life, and malnutrition on treatment outcomes and TB treatment-associated adverse events.
2. To assess the genotype-phenotype correlation among resistant TB isolates through MIC-based phenotypic drug susceptibility testing and next generation sequencing of TB isolates, including assessment of strain evolution, drug susceptibility pattern changes during treatment, and impact of strain on treatment outcomes.
3. To derive pharmacokinetic parameters of second-line agents in participants receiving multidrug treatment regimens with particular attention to linezolid, clofazimine, high-dose moxifloxacin, aminoglycosides, and any new drugs that become available including bedaquiline and delamanid.
4. To assess host biomarkers of treatment response and correlates of progression from exposure to TB disease using multiomics approaches (e.g. transcriptomics, metabolomics, cellular markers, and immunity- and inflammation-associated soluble biomarkers).
5. To assess microbial markers of treatment response including smear and culture conversion, quantitative burden, and the time to conversion.
6. To assess standard and novel imaging approaches to monitor treatment responses.
7. To assess the impact of TB on the quality of life and mental health of subjects with MDR-TB, and in turn their impact on treatment adherence and outcomes.
8. To assess host immune responses to and inflammation following TB exposure and TB treatment and correlate these responses with clinical outcomes.
9. To ascertain true outcomes and self-reported barriers to treatment retention of MDR-TB participants lost to follow-up (≥2 consecutive months of missed visits) during treatment through prospective phone follow-up and/or home visits.

CONTINUED: MDR-TB Free: Monitoring Adverse Effects, Utilizing Resources Optimally, Knowing Resistance Patterns, and Treatment Strategy (MDR TB MUKT)

Cohort B Secondary Objectives

1. To determine the feasibility of enrolling household contacts of index adult MDR TB cases.
2. To explore the proportion of contacts with prevalent TB disease and infection, what proportion develop new TB disease and infection during follow-up, and what are prevalent comorbidities (diabetes mellitus, prediabetes, HIV, COPD, smoking status, alcoholism, depression, quality of life, and malnutrition) among the household contacts.
3. To contribute samples to a global repository for the study of biomarkers of incident TB and progression from exposure to TB disease using multiomics approaches (e.g. transcriptomics, metabolomics, cellular markers, and immunity- and inflammation-associated soluble biomarkers)

Status: Data analysis ongoing

Publication: Udwadia ZF, Tornheim JA, Ganatra S, DeLuca A, Rodrigues CS, Gupta A. Few eligible for the newly recommended short course MDR-TB regimen at a large Mumbai private clinic. *BMC Infect Dis.* 2019 Jan 28;19(1):94. doi: 10.1186/s12879-019-3726-8. PMID: 3069140

Publication: Tornheim JA, Intini E, Gupta A, Udwadia ZF. Clinical features associated with linezolid resistance among multidrug resistant tuberculosis patients at a tertiary care hospital in Mumbai, India. *J Clin Tuberc Other Mycobact Dis.* 2020 Jul 24;20:100175. doi: 10.1016/j.jctube.2020.100175. eCollection 2020 Aug. PMID: 3277570

Publication: Tornheim JA, Udwadia ZF, Arora PR, Gajjar I, Sharma S, Karane M, Sawant N, Kharat N, Blum AJ, Shivakumar SVBY, Gupte AN, Gupte N, Mullerpattan JB, Pinto LM, Ashavaid TF, Gupta A, Rodrigues C. Increased Moxifloxacin Dosing Among Patients With Multidrug-Resistant Tuberculosis With Low-Level Resistance to Moxifloxacin Did Not Improve Treatment Outcomes in a Tertiary Care Center in Mumbai, India. *Open Forum Infect Dis.* 2021 Dec 23;9(2):ofab615. doi: 10.1093/ofid/ofab615. eCollection 2022 Feb. PMID: 35097152 Free PMC article.

Publication: Tornheim JA, Udwadia ZF, Arora PR, Gajjar I, Gupte N, Sharma S, Karane M, Sawant N, Kharat N, Blum AJ, Shivakumar SVBY, Mullerpattan JB, Pinto LM, Ashavaid TF, Gupta A, Rodrigues C. Cycloserine did not increase depression incidence or severity at standard dosing for multidrug-resistant tuberculosis. *Eur Respir J.* 2022 Mar 24;59(3):2102511. doi: 10.1183/13993003.02511-2021. Print 2022 Mar. PMID: 34949698 Free PMC article.

Publication: Resendiz-Galvan JE, Arora PR, Abdelwahab MT, Udwadia ZF, Rodrigues C, Gupta A, Denti P, Ashavaid TF, Tornheim JA. Pharmacokinetic analysis of linezolid for multidrug resistant tuberculosis at a tertiary care centre in Mumbai, India. *Front Pharmacol.* 2023 Jan 4;13:1081123. doi: 10.3389/fphar.2022.1081123. eCollection 2022. PMID: 36686664 Free PMC article.

Publication: Lokhande RV, Arora PR, Joubert A, Bhagure GR, Udwadia ZF, Gupta A, Rodrigues C, Tornheim JA, Wiesner L, Ashavaid TF; MDR-TB MUKT and RePORT India Study Team; Indo-South Africa Study Team. Quantitation of Plasma Bedaquiline Concentrations in Indian MDR-TB Patients Using Liquid Chromatography-Tandem Mass Spectrometry. *Biomed Chromatogr.* 2025 Dec;39(12):e70243. doi: 10.1002/bmc.70243. PMID: 41235782

Publication: Resendiz-Galvan JE, Arora PR, Lokhande RV, Udwadia ZF, Rodrigues C, Gupta A, Tornheim JA, Denti P, Ashavaid TF; The MDR-TB MUKT and Indo-South Africa Study Teams; Evaluation of cycloserine dose regimens in an Indian cohort with multidrug-resistant tuberculosis: a population pharmacokinetic analysis. *Antimicrob Agents Chemother.* 2025 Oct;69(10):e0010125. doi: 10.1128/aac.00101-25. Epub 2025 Sep 2. PMID: 40891988 Free PMC article.

CONTINUED: MDR-TB Free: Monitoring Adverse Effects, Utilizing Resources Optimally, Knowing Resistance Patterns, and Treatment Strategy (MDR TB MUKT)

- **Manuscript Submitted:** Lokhande RV, Arora PR, Bhagure GR, Joubert A, Udwadia ZF, Rodrigues C, Gupta A, Mave V, Raichur P, Gaikwad S, Khan R, Pradeep A, Wiesner L, Tornheim JA, Horsburgh CR, Ashavaid TF for the MDR-TB MUKT and RePORT India Team, Indo-South Africa Study Team and PREEMPT Study Teams. Analytical method development and validation for clofazimine in human plasma and application of LC-MS/MS based methods for clofazimine and bedaquiline in Indian MDRTB patients stratified by HIV coinfection.
- **Manuscript Submitted:** Nkuhairwe IN, Arora PR, Lokhande RV, Resendiz-Galvan JE, Yadav P, Verma R, Wiesner L, Keny B, Udwadia ZF, Rodrigues C, Denti P, Tornheim JA, Wasmann RE, Ashavaid TF for the MDR-TB MUKT and Indo-South Africa Study Teams. Model-based evaluation of amikacin and ethambutol dosing strategies in Indian patients with multidrug-resistant tuberculosis.
- **Abstracts:**
 - A. Suresh, Z.F. Udwadia, S. Pinto, U. Rudra, P.R. Arora, A. Gupta, J. Mullerpattan, L. Pinto, T.F. Ashavaid, C. Rodrigues, J.A. Tornheim, MDR TB MUKT study team. Association of PAS and Ethionamide with hypothyroidism and treatment outcomes in MDR-TB Patients in India (Abstract Accepted to Union Conference on Lung Health 2026)
 - M. Chaturvedi, Z.F. Udwadia, M. Amirapu, P.R. Arora, A. Gupta, M. Proschian, M. Manion, C. Rodrigues, T. Ashavaid, L. Pinto, J.A. Tornheim Longitudinal Associations of Clinical Variables and Chest Imaging with Respiratory Symptom Burden in Drug-Resistant Tuberculosis (Abstract Accepted to Union Conference on Lung Health 2026)
 - P Yadav, S Shah, AS Babu, M Paradkar, S Vasanthaiah, P Denti, C Rodrigues, JR Andrews, A Pandey, JA Tornheim, TF Ashavaid, R Verma, MDR TB MUKT study team. Development of a Nanopore sequencing panel for saliva-based screening of host TB pharmacogenomic markers (Abstract Accepted to Union Conference on Lung Health 2026)

Dynamics and Immune Mechanisms of QFT Response in Close Contacts of TB Cases

Principal Investigators	Site	Population	Funding
Padmini Salgame (Rutgers)	JIPMER	HHCs of TB patients	NIH
Sonali Sarkar (JIPMER)	BJGMC		
Vidya Mave (BJGMC)			

Design: Establish a prospective observational cohort of 1000 household contacts (HHC) of TB patients at JIPMER and BJMC. The proposed cohort will be classified after 12 months of follow-up into four groups: sustained QFT negatives, sustained QFT positives, QFN converters and QFN reverts.

Objectives:

1. Determine the clinical implications of dynamic changes in the QFT response in 12 months following close contact with a TB patient.
2. Examine if dynamic changes in the QFT response are associated with activation of phenotypically and functionally distinct subsets of T cells.
3. Examine if the dynamic changes in the QFT response are associated with altered macrophage anti-mycobacterial effector responses.

Status: Enrollment and follow-up completed. Assays underway

Analysis of Host Biomarkers Associated with Adverse TB Treatment Outcomes Across RePORT International Sites

Principal Investigators			Funding
Sheetal Verma (Rutgers)	Beatriz Barreto-Duarte (Oswaldo Cruz Foundation, Brazil)	Erlina Burhan (INA RESPOND, Persahabatan Hospital)	RiCC
Senbagavalli Prakash Babu (JIPMER)	Simon Mendelsohn (South African Tuberculosis Vaccine Initiative)	Sri Ram Pentakota (Rutgers)	
Artur Queiroz (Oswaldo Cruz Foundation, Brazil)	John Carlo Malabad (University of Philippines-Manila)	Dr. Arthur Vanvalkenburg (Rutgers)	
Mariana Araújo-Pereira (Oswaldo Cruz Foundation, Brazil)			

Design: Host biomarkers will be assessed in nested case-control cohorts using archived Paxgene RNA and plasma samples from Common protocols that were collected at baseline and treatment month 2 and 6; Participants with microbiological treatment failure or recurrence will be matched 1:2 with controls with lasting cure. Samples from EOT will assess the risk of recurrence after cure. Testing at baseline addresses response prediction prior to ATT initiation. Month-2 evaluates response kinetics, that may provide insights into mechanisms of treatment failure when analyzed in the context of host and microbial parameters. Testing at month-6 is an approach to confirm cure and predict recurrence at ATT completion.

Aims:

1. To validate a small panel of host blood RNA signatures that predict the outcome of tuberculosis treatment using the Fluidigm (Standard Biotoools™) platform.
2. To develop a parsimonious and generalizable signature of failure from a large panel of existing signatures using the digital NanoString platform.
3. To validate host blood protein signatures that predict the outcome of tuberculosis treatment using Luminex platform and derive a reduced proteome signature.
4. To develop a novel "cure" signature using RNA-seq as a discovery-based approach.

Status: Analysis in progress

Identifying TB Treatment Response Biomarkers Using qRT-PCR Signature for TB Treatment Response and TB NanoString for Tx

Principal Investigators	Funding
Hardy Kornfeld (UMass)	RiCC
Padmini Salgame (Rutgers)	

Design: To validate five signatures (RESPONSE5, ACS6, RISK4, Khatri 3-gene, and Maertzdorf4-gene) as blood biomarkers in predicting TB treatment response to favorable and unfavorable treatment outcomes in the RePORT cohorts

Aims: To develop a promising blood biomarker for identifying response to TB treatment among active TB cases

Status: Study on hold because initial funding used up by the NanoString study

Rapid Research in Diagnostics Development for TB Network (R2D2 TB Network) Study

Principal Investigators	Sites	Population	Funding
D.J. Christopher (India)	CMC Vellore, India	Adult outpatients (age ≥ 18	NIH
Adithya Cattamanchi (USA)	Hanoi Lung Hospital, Vietnam	years) with cough ≥ 2	
Payam Nahid (USA)	De La Salle Medical and	weeks' duration, a	
Claudia Denkinge (Germany)	Health Sciences Institute,	commonly accepted	
	Philippines Stellenbosch	criterion for identifying	
	University, SA Makerere	patients with presumed	
	University College of Health	pulmonary TB	
	Sciences, Uganda		

Design: For the novel TB triage and diagnostic tests, we will conduct large-scale evaluation of design-locked tests in a cohort of adults with presumed TB, with nested feasibility/pilot studies of early and late prototype tests. The large-scale evaluation is a prospective cross-sectional study of 3,000 participants (600/clinical study site).

Objectives:

1. To conduct pilot studies of the diagnostic accuracy and usability of early and late prototypes of novel TB tests in settings of intended use to inform their further development.
2. To conduct large-scale validation studies of the diagnostic accuracy and usability of design- locked novel TB tests to inform policy development.

Our study hypotheses are:

1. Early and late prototypes of novel TB tests will meet pre-specified decision thresholds for advancement to the next phase of assessment.
2. Design-locked novel TB tests will meet updated WHO target product profile (TPP) requirements for minimum diagnostic accuracy.

Status: Phase 1 Completed, RePORT India not a part of Phase 2

Publication: Yerlikaya S, Chirwa M, Ajide B, Castro MDM, Ha H, Kato-Maeda M, Kisakye E, Marcelo D, Mochizuki T, Rockman L, Steadman A, Thangakunam B, Bimba JS, Christopher DJ, Muyoyeta M, Phan H, Theron G, Yu C, Kremer K, Phillips PPJ, Nahid P, Denkinge CM, Cattamanchi A, Andama A; R2D2 TB Network and SMART4TB Consortia. Pulmonary Tuberculosis Detection with MiniDock MTB Using Swab Samples. *N Engl J Med.* 2026 Apr 30;394(17):1710-1722. doi: 10.1056/NEJMoa2509761. PMID: 42054680; PMCID: PMC13132025.

Whole Genome Sequencing of Drug Resistant Tuberculosis in India: Genotype-Phenotype Correlation, Clinical Impact of Resistance, and Sequencing Directly from Sputum (K23)

Principal Investigators	Sites	Population	Funding
Camilla S. Rodrigues (Hinduja)	Hinduja	Cohort A (MDR-TB MUKT): Adults and adolescents ≥ 15 years of age with MDR-TB (n=200)	NIH: K23
Jeffrey A. Tornheim (JHU)			

Design: The K23 analysis will correlate mutations identified by whole genome sequencing with both MGIT and MIC drug susceptibility test results, correlate those results with plasma drug levels and participant outcomes, and compare the results obtained by sequencing the isolates without culture to those obtained by sequencing MGIT cultures and solid cultures.

Aims

1. Characterize MIC distribution for mutations identified on WGS in Indian MDR-TB strains and compare the frequency and predictive value of WGS-derived mutations in Mtb isolates from Indian MDRTB patients with those from South African MDR-TB patients in the ReSeqTB Data Platform.
2. Assess the impact of partial resistance (identified by WGS and MIC-testing) and drug exposures (using PK-PD analysis) on patient outcomes in a cohort of MDR-TB patients.
3. Assess a new direct-from-sputum method for WGS compared to culture-based WGS for DST.

Status: Sample processing completed; Manuscript draft underway

Validation of SpitSeq Assay

Abstract: Diagnostic performance of a direct-from-sputum next generation sequencing method for prediction of phenotypic resistance to second-line tuberculosis drugs, Union World Conference on Lung Health, Bali, Indonesia, 11-Nov-24

Manuscript Drafted: Planned for resubmission in 2026: Diagnostic performance of direct-from-sputum whole genome sequencing for prediction of phenotypic resistance in Mycobacterium tuberculosis

Manuscript Drafted: Planned for submission in 2026: Determination of the mid-treatment molecular clock for MDR-TB: Evaluation of the rate of mutation acquisition in SNP/month and SNP/year within each study participant using serial sequencing of mid-treatment isolates, accounting for differences in individual treatments received during each sampling interval

SUBSTUDIES

Abdominal and Thoracic Ultrasound for the Diagnosis of Pulmonary and Extra-pulmonary Tuberculosis. Assessing the Accuracy of Point-of-care Ultrasound for the Diagnosis and Therapy Monitoring in Patients with Presumed Tuberculosis in India and Germany

Principal Investigators

D.J. Christopher (India)
Claudia M. Denking (Germany)

Sites

CMC Vellore, India
Heidelberg University, University Clinics Cologne
University Clinics Frankfurt, Germany

Population

Patients aged 18 years or older presenting with: clinical constellation compatible with Pulmonary (PTB) and extra-pulmonary TB (EPTB)

Design: A prospective, multicentre study (Germany, India), we will enroll patients with presumed active TB of any anatomic site and in both in- and outpatient settings.

Objectives:

- To assess the accuracy of the FASH-protocol for diagnosing TB in extra-pulmonary sites (i.e. abdominal lymph nodes, splenic micro-abscesses, pleural or pericardial effusions, liver micro-abscesses) using a microbiological reference standard (MRS), an extended microbiological (eMRS) and composite reference standard (CRS) in presumptive adult TB-patients in Germany and separately in India
- To assess the accuracy of lung ultrasound for the diagnosis of pulmonary tuberculosis (unilateral large pleural effusion, especially with stranding, subpleural nodules (SUN) pattern, consolidation with an additional sign of TB (SUN, abdominal nodes, splenic lesions, pericardial effusions)) using a microbiological (MRS), extended microbiological (eMRS) and composite reference standard (CRS) in presumptive adult TB-patients in Germany and separately in India

Status: Phase 1 Completed, RePORT India not a part of Phase 2

Publication: Weber SF, Wolf R, Manten K, Thangakunam B, Isaac B, Shankar D, Mangal D, Dutta AK, Vimala LR, Irodi A, Tobian F, Koepfel L, Beck JS, Wolf P, Bélard S, Denking CM, Christopher DJ; ALL POCUS TB India study group. Lung and abdominal ultrasound accuracy for tuberculosis: An Indian prospective cohort study. PLoS One. 2025 Sep 3;20(9):e0329670. doi: 10.1371/journal.pone.0329670. PMID: 40901833; PMCID: PMC12407472.

Innate immune response of LTBI+HIV+ children

Principal Investigators

Ramakrishna Vankayalapati

Funding

NIH R01

Description: Mycobacterium tuberculosis (Mtb) infects one-third of the world's population and causes almost 1.3 million deaths per year, including 100,000 children. Approximately 90% of infected persons have latent tuberculosis infection (LTBI), have protective immunity and remain well, but 10% develop primary tuberculosis (TB) soon after infection or reactivation TB many years later. TB is the leading cause of death in HIV-infected persons and more than half a million coinfecting people die annually. Children are more susceptible to TB infection, due to an immature immune system. HIV infection in children markedly increases susceptibility to TB. To develop adequate prophylaxis or therapy, it is important to understand immune responses to Mtb. Identification of HIV+ children with LTBI who are at greatly increased risk for development of TB would allow treating only high-risk children, facilitating completion of therapy for LTBI and preventing future development of TB. To identify these children, it is important to pinpoint the nature of the defective immune responses that permit development of active TB in HIV+LTBI+ pediatric patients. This proposal will identify a novel memory-like NK cell subpopulation mediated mechanisms that regulate immune responses and pinpoint the nature of the defective responses that permit development of active TB in HIV-LTBI+ and HIV+LTBI+ children. These studies will lay the groundwork for strategies to develop novel anti-tuberculosis vaccines that stimulate strong NK cell mediated immunity in HIV+ and HIV- children with LTBI, and reduce development of TB

Status: Study ongoing; preparation of 4 manuscripts underway

Pharmacokinetic Assessment of MDR-TB Drugs in the Treatment of TB Meningitis (MDR-TBM PK)

Principal Investigators	Sites	Population	Funding
Jeffrey A Tornheim (JHU)	BJGMC	Adult MDR TBM patients on TB treatment (N=70 all sites)	CRDF Global
Tester F. Ashavaid (Hinduja)	Hinduja	- (Hinduja site n=20)	
Hongfei Duan (Beijing Chest Hospital)	International Sites		
Ebrahim Variava (Perinatal HIV Research Unit)	Johns Hopkins		
Rohidas Tanku Borse (BJGMC)	Beijing Chest Hospital PHRU		
	Wits Health		

Design: Patient suspected of TBM will be screened for the eligibility of enrolment in the study. Eligible participants will be consented, enrolled and followed up for a 6-month period after enrollment with a total of 8 clinical encounters each. On enrolment, a baseline lumbar puncture (LP) will be performed to confirm the diagnosis of TBM. If suspected patients have already undergone an LP, the sample will be retrieved from the labs and stored for biorepository. This LP will be a part of standard of care (SOC). For the PK studies, participants will be followed up for Week 1 G Week 4 with repeat LP. These LP may be as a part of SOC or for research use only for PK studies.

Aims:

1. Penetration coefficient of each drug into the CSF
2. Relationship between PK parameters, survival, and functional status.

Status: Data analysis and manuscript preparation ongoing

Manuscript Under Review: Tornheim JA, Calderin JM, Upton CM, Castel S, Wiesner L, Dooley KE, Denti P. Cerebrospinal fluid penetration of pyrazinamide, levofloxacin, and linezolid in patients with pulmonary tuberculosis.

Baseline pRescription According to Direct from Sputum Sequencing and Targeted drug Concentration Strategy (BRASS TACS)

Principal Investigators	Site	Population	Funding
Tester F. Ashavaid (Hinduja)	Hinduja	Adult with Pulmonary RR/MDR-TB (n=210)	NIH: R01
Camilla S. Rodrigues (Hinduja)			
Zarir F. Udwadia (Hinduja)			
Jeffrey A. Tornheim (JHU)			

Design: This study is an observational study of a combined treatment strategy informed by NGS, TDM, and MIC testing. The study will enroll adults starting treatment at Hinduja Hospital for RR/MDR-TB of the lungs. All data will be provided to clinicians to help personalize therapy. Outcome and side effect data will be compared to data from historical controls with MDR-TB enrolled in previous RePORT-India associated cohort studies at Hinduja Hospital using propensity score matching by disease severity and resistance to assess the impact of the BRASS TACS treatment strategy to outcomes among similar patients treated without this strategy.

Aims:

1. To determine the proportion of patients with MDR-TB in Mumbai, India with resistance-associated mutations that would prevent treatment with moxifloxacin, linezolid, bedaquiline, clofazimine, or cycloserine using culture-free NGS.
2. To identify the proportion of cohort participants with MDR-TB that achieve model-derived steady-state plasma levels meeting efficacy and toxicity targets.
3. To assess the time to final regimen, frequency of treatment-associated side effects, time to culture conversion, and final outcome of cohort participants who complete culture-free NGS and TDM.

Status: Enrollment ongoing. tNGS, WGS, MIC testing, TDM, PK modeling, pharmacogenomic analyses, vDOT monitoring, and pulmonary function testing are underway. Preliminary analyses for resistance prediction and drug exposure outcomes are planned for 2026. Manuscripts and abstracts are anticipated following completion of initial analyses.

Identification of *M. tuberculosis* and Prediction of Drug-resistance among Adults with Pulmonary Tuberculosis Using a Novel Urine Collection and Target Concentration Device, Followed by Cartridge-based Nucleic Acid Amplification Testing (Urigami and CBNAAT Study)

Principal Investigators	Site	Population	Funding
Tester F. Ashavaid (Hinduja) Camilla S. Rodrigues (Hinduja) Jeffrey A. Tornheim (JHU)	Hinduja	1. Adult PTB MDR patients on TB treatment (N=400 for India and 200 for Brazil) 2. Adult healthy contacts (n=Up to 20)	CFAR NIH: R21

Design: We will transfer the novel urine capture and affinity bait method developed at the Liotta Lab in the USA to the PD Hinduja National Hospital and Medical Research Centre in Mumbai, India where it will be used to assess the baseline and 6-month urine samples collected from newly diagnosed adults with drug susceptible pulmonary tuberculosis, as well as the de-identified baseline and 6-month urine samples collected from participants in the MDR-TB MUKT cohort with pulmonary MDR-TB and fluoroquinolone resistance stored in the MDR-TB MUKT biorepository. Specificity will be assessed by repeating the assay among de-identified samples collected from household contacts of pulmonary TB patients stored in the MDR-TB MUKT biorepository.

Aims:

1. To assess the diagnostic accuracy of the combination of a collapsible urine collection device with hydrogel nanocage affinity baits for *Mtb* cfDNA and the Xpert MTB/RIF and Xpert Ultra for the detection of pulmonary *Mtb* and rifampin resistance from freshly collected urine.
2. To assess the accuracy of this combination method to identify resistance to isoniazid, fluoroquinolones, and second-line injectable drugs using the Xpert XDR cartridge on de-identified samples in a well-characterized biorepository.
3. To implement this novel concentration technology in a high burden setting by transferring technology developed in a US laboratory to the Indian context. To achieve an analytical sensitivity for genomic DNA of 10 pg/mL in urine matrix.

Status: Study stopped due to lack of funding

CRISPR - Multiplexed detection of cell-free *M. tuberculosis* DNA and its drug-resistant variants in blood

Principal Investigators	Site	Population	Funding
Prerna Arora (Hinduja) Jeffrey A Tornheim (JHU) Tony Hu (Tulane)	Hinduja Tulane JHU	Adults with drug resistant and drug susceptible disease and their household contacts	NIH R01

Design: A diagnostic accuracy and treatment response study nested within MDR-TB MUKT and BRASS TaCS to evaluate a novel assay to detect cell-free *Mtb* DNA fragments in the blood of people with active tuberculosis, to evaluate the ability of the same assay to detect markers of drug-resistance, and to assess the response to successful treatment using biorepository specimens.

Aims:

1. To optimize our CRISPR-TBD POC assay to analyze *Mtb*-cfDNA in blood samples.
2. To evaluate the performance of the CRISPR-TBD assay for TB diagnosis and treatment evaluation.
3. To conduct an in-field validation of the multiplex CRISPR-TBD POC assay in an Indian clinical laboratory whose population faces a high burden of drug resistant TB

Status: Assay optimization and pilot validation completed; prospective clinical validation using MDR-TB cohort samples underway. Longitudinal sample testing and analysis ongoing, with manuscript and abstract development planned following completion of validation analyses.

InTGS: Whole Genome Sequencing of MTB Clinical Strains for Determining Drug Resistance and Strain lineage in India: A Structured Nationwide Approach

Principal Investigators	Site	Population	Funding
Sonali Sarkar (JIPMER)	JIPMER, NII,	Cohort A participants of parent	DBT
Vinay Kumar Nandicoori (CCMB)	ICGEB,	protocol from JIPMER, CMC,	
Dhiraj Kumar (ICGEB)	CCMB,	NIRT and BJGMC	
G. Aneeshkumar Arimbasseri (NII)	NIBMG,	Microbiologically confirmed TB	
Arindam Maitra (NIBMG)	BMMRC,	patients from participating sites	
Camilla Rodrigues (Hinduja)	BJGMC, PGI,		
S. Siva Kumar (NIRT)	Hinduja, NIRT		
Vijaya Valluri (BMMRC)			

Design: We propose to use both retrospective and prospective approaches for sample collection. Retrospective approach will use samples collected under the Regional Prospective Observational Research in Tuberculosis (RePORT) India studies or samples (sputum/extra pulmonary specimens) from studies involving TB positive patients (smear/CBNAAT/TrueNat) from participating institutions. Prospective samples (MTB positive sputum/extra-pulmonary specimens), will be obtained from selected Intermediate Reference Laboratories (IRL) culture drug susceptibility testing (C-DST) centers and in-patient and out-patient departments of participating hospitals/institutions

Aims:

1. To perform WGS of 32,200 clinical strains from active TB patients and to develop a centralized biorepository of clinical MTB strains in India.
2. To map genetic diversity of pulmonary and extrapulmonary isolates of MTB from newly reported active TB cases in India and the associated treatment outcomes.
3. Association of mutations of MTBC to phenotypic drug resistance patterns.
4. To combine epidemiological data with WGS results to extract actionable public health data-driven information

Status: Preliminary genomic analyses completed for processed samples., a consortium-wide manuscript is under preparation. and a JIPMER site-specific manuscript is also being developed for publication.

Understanding Mycobacterium tuberculosis Mediated Host Metabolomics in Pulmonary Tuberculosis: Correlation with Disease Severity and Treatment Course

Principal Investigators	Sites	Population
Senbagavalli Prakash Babu (JIPMER)	JIPMER	Adult participants enrolled in the Active TB cohort (Cohort A) and Household contact (Cohort B) of common protocol phase I
Sonali Sarkar (JIPMER)	IISER	

Design: We will use plasma samples collected from common protocol cohorts to measure the metabolomic markers; active pulmonary TB (n=20) grouped as per disease severity (mild and severe) and their household contacts (n=10). For cohort A participants, samples will be analyzed at baseline, Month 1 and End of treatment; for cohort B at baseline

Aims

1. To study the differences in MTB influenced host metabolomics in mild and severe disease groups.
2. To study the dynamic changes of host metabolites at baseline, during and at the end of the standard anti-TB treatment regimen.
3. To examine whether there is a correlation between host metabolomics with disease severity and course of standard anti-TB treatment.

Status: Study completed.

Publication: Kagemann CH, Prakash Babu S, Ezhumalai K, Chakraborty A, Raghupathy K, Kamat SS, Viswanathan V, Huey SL, Narasimhan PB, Sinha P, Yu EA, Mehta S, Sarkar S; Regional Prospective Observational Research on Tuberculosis India Consortium. Metabolite dynamics over the course of anti-tuberculosis treatment in individuals with mild and severe tuberculosis. PLOS Glob Public Health. 2025 Oct 15;5(10):e0004925. doi: 10.1371/journal.pgph.0004925. PMID: 41091730; PMCID: PMC12527214.

Evaluating the clinical utility of a novel RNA based assay for predicting TB treatment outcomes and diagnosing paucibacillary TB

Principal Investigators	Sites	Funding
Kayvan Zainabadi (Cornell U) Rajesh Karyakarte (BJGMC) Sanjay Gaikwad (BJGMC) Amita Gupta (JHU) Neeta Pradhan (BJGMC) Mandar Paradkar (BJGMC) Vidya Mave (BJGMC)	Cornell University, BJGMC and JHU for RePORT India; Makerere University for RePORT Uganda	RICC

Population: For treatment outcomes we will examine RePORT India TB cohorts who were on standard 6-month first-line therapy and who were followed for 16 months for clinical outcomes (cure, treatment failure, or recurrent TB). For paucibacillary TB we will examine a pediatric TB cohort from RePORT Uganda who were followed for up to 24 months for TB diagnosis (confirmed, unconfirmed, or unlikely TB).

Design: This study is taking place entirely in-country at RePORT India at BJGMC in Pune, India and RePORT Uganda at Makerere University in Kampala, Uganda and is expected to take 2 years to complete. We are utilizing a newly published ultrasensitive Mtb 16S rRNA assay that is capable of distinguishing live from dead Mtb and detecting viable but not culturable Mtb which culture misses. We will examine whether this new RNA-based test can identify culture-negative patients who later go on to experience poor treatment outcomes (failure or recurrent TB) or who harbor paucibacillary TB.

Aims:

1. Assessing the clinical utility of the Mtb 16S rRNA-based assay to predict treatment outcomes (India).
2. Assessing the clinical utility of the Mtb 16S rRNA-based assay to detect paucibacillary TB (Uganda).
3. 3) Identify quantitative threshold values that improve the diagnostic accuracy of the assay for predicting treatment outcomes in a discovery cohort and then confirm the utility of the refined assay for predicting outcomes in an independent cohort (India).
4. Identify quantitative threshold values that improve the diagnostic accuracy of the assay for detecting paucibacillary tuberculosis in a discovery cohort and then confirm the utility of the refined assay for detecting paucibacillary tuberculosis in an independent validation cohort (Uganda).
5. Capacity building and technology transfer to RePORT India and Uganda

Status: Ethical approval has already been obtained and all samples for both studies have already been identified and QCed. Kayvan Zainabadi made an initial visit to RePORT India in April 2025 and subsequently in Sep-Oct 2025 to setup and initiate the project. All equipment, supplies and reagents were put in now in place, training of the BJGMC CRS TB laboratory team was completed, sample assays were performed on the training and test cohorts to generate initial data for confirmed recurrences and controls. These data are being analysed, interim analysis was presented on RICC research call, March 2026. Further analysis is ongoing and testing of remaining samples will be completed in quarter 3 and 4, 2026.

Aim 1: Diagnostics: evaluate novel diagnostics & biomarkers of diverse states of MTB infection

TB NanoString Transcriptomics

Aim: To utilize NanoString technology to measure mRNA expression levels of TB-associated gene signatures, aiming to derive a parsimonious TB signature for distinguishing incipient, subclinical, and active TB disease.

Diagnosis of Incident TB Infection (TBI)

Aim: To evaluate the ability of TB NanoString and plasma cytokine profiles to distinguish recent TB infection (incident TBI) from stable IGRA-positive and IGRA-negative individuals. The goal is to improve risk stratification for disease progression by identifying sensitive and specific biomarkers of recent infection.

Diagnostic Cohort Principal Investigators: Tester F. Ashavaid (Hinduja), Camilla S. Rodrigues (Hinduja), Jeffrey A. Tornheim (JHU)

Status: Completed enrollment. Manuscript preparation underway.

Proposed Manuscript: Identification of recent TBI using NanoString and cytokine profiles.

Cohort B Principal Investigators: Tester F. Ashavaid (Hinduja) Camilla S. Rodrigues (Hinduja) Jeffrey A. Tornheim (JHU)

Cohort B Status:

- Enrolled 122 participants in a cohort of household contacts of adults with pulmonary drug resistant tuberculosis
- Developed a technical control for NanoString profiling at the individual level to classify each participant as evidencing gene expression "more similar to people with TB" or "more similar to people without TB"
- Completed NanoString profiling of baseline samples of all 122 household contacts to assign that classification
- Completed PET scans at the time of enrollment for 10 participants and to evaluate longitudinal changes.
- Will be correlating NanoString and PET results to determine if NanoString gene expression profiling can serve as an accurate classifier of TB risk after exposure to DR-TB.
- Final analysis is ongoing.

Aim 1: Diagnostics: evaluate novel diagnostics & biomarkers of diverse states of MTB infection *Continued*

Plasma Triage

Aim: To develop and validate plasma metabolomic signatures as a non-sputum triage tool for distinguishing tuberculosis from non-TB respiratory illness and to identify metabolic biomarkers predictive of treatment response and unfavorable outcomes using longitudinal plasma samples..

Proposed Manuscript: Plasma metabolomic signatures as a non-sputum triage tool for tuberculosis in presumptive TB patients

Status: Baseline plasma samples from microbiologically confirmed TB patients and non-TB respiratory controls have been identified. Sample pre-processing has been completed at JIPMER, and the processed samples have been shipped to IIT Mumbai for LC-MS-based metabolomic profiling. Metabolomic profiling has been completed. Bioinformatic and statistical analyses are currently underway to identify metabolite signatures capable of discriminating microbiologically confirmed TB from non-TB respiratory illness. Manuscript preparation will commence following completion of the data analysis.

Proposed Manuscript: Longitudinal plasma metabolomic signatures associated with tuberculosis treatment response and unfavorable clinical outcomes.

Status: Longitudinal plasma samples from RePORT India Cohort A have been selected and pre-processed at JIPMER. Metabolomic profiling of longitudinal plasma samples has been completed. Integrated bioinformatic analyses correlating metabolic signatures with treatment response, disease severity, and clinical outcomes are currently in progress. Manuscript writing will begin after completion of the final analyses.

Aim 1: Diagnostics: evaluate novel diagnostics & biomarkers of diverse states of MTB infection *Continued*

Computer-Aided Diagnosis (CAD)

Aim: To leverage artificial intelligence-driven CAD systems to analyze digitized chest radiographs within the RePORT India consortium, improving the accuracy and efficiency of early TB detection.

Principal Investigators: Aarti Kinikar (BJGMC-JHU CRS) Mandar Paradkar (BJGMC-JHU CRS) Sanjay Gaikwad (BJGMC) Amita Gupta (JHU), Vidya Mave (BJGMC-JHU CRS)

Status: In the process of procuring the AI software

Proposed Manuscript, Adult: Artificial Intelligence in Tuberculosis Diagnosis: Enhancing Accuracy and Speed with Computer-Aided Diagnosis Systems; Deep Learning Models for Tuberculosis Diagnosis: A Study on the Application of AI to Digitized Chest Radiographs

Proposed Manuscript, (CAPTURE Consortium study) Pediatric: Artificial Intelligence in Tuberculosis Diagnosis: Enhancing Accuracy and Speed with Computer-Aided Diagnosis Systems; Deep Learning Models for Tuberculosis Diagnosis: A Study on the Application of AI to Digitized Chest Radiographs

Status:

- Final analysis is nearing completion, and manuscript is being prepared in parallel for publication of the primary results.
- Abstract presented at the 2025 Union as a late breaker (Mikashmi Kohli) and part of a Union Symposium session.
- For the 'objective 3' of sharing CXRs with developers for CAD software optimisation – all partners will receive updated agreements for their review and signature to allow for inclusion of their data in this step.

Publication: Palmer M, Kik SV, Kohli M, Fataar A, Anyebe V, Frey N, Castro R, Nerurkar R, van der Westhuizen JN, Macé A, Ruhwald M, Seddon JA, Jaganath D; CAPTURE Consortium group. Catalysing Artificial Intelligence for Paediatric Tuberculosis Research (CAPTURE): protocol for a global multicentre study establishing a paediatric chest X-ray repository to evaluate computer-aided detection algorithms. *BMJ Open*. 2026 Jan 12;16(1):e108668. doi: 10.1136/bmjopen-2025-108668. PMID: 41526020; PMCID: PMC12815126.

Aim 2: Markers of treatment response

2A: Identify TB treatment response biomarkers

TB NanoString for Treatment Response

Aim: To optimize and test a concise NanoString panel for TB diagnosis in an Indian population and evaluate its performance in monitoring treatment response.

Principal Investigator: Padmini Salgame (Rutgers U)

Proposed Manuscript: Validation of NanoString Platform for TB Treatment Response Biomarkers in India

Status:

- Sample testing using the NanoString platform has been completed.
- Complementary total RNA seq was performed on RNA extracted from PaxGene tubes to expand transcriptomic coverage.
- Integrated data analysis is underway, and manuscript preparation has begun.

DR-TB RNA Treatment Response Signatures

Aim: To assess the utility of RNA signatures in monitoring treatment response in drug-resistant TB (MDR-TB, pre-XDR-TB, and XDR-TB) and compare their performance across different resistance profiles and treatment time points.

Principal Investigators: Tester F. Ashavaid (Hinduja), Camilla S. Rodrigues (Hinduja), Jeffrey A. Tornheim (JHU)

Proposed Manuscripts:

1. Early Detection of Treatment Response in Drug-Resistant TB Using RNA Signatures
2. Identification of the most useful timepoints to evaluate those biomarkers of DR-TB treatment response
3. Validation of NanoString Platform for TB Treatment Response Biomarkers in India

Status: NanoString and cytokine profiling done, analysis on going for 3 manuscripts

Plasma Cytokine for Treatment Response

Aim: To evaluate plasma cytokine signatures as potential biomarkers for TB treatment response, using multiplex analysis to assess their association with treatment outcomes.

Principal Investigator: Pavan Kumar (NIRT)

Manuscript Submitted: Validation of Immune Biomarkers for Pulmonary Tuberculosis to Identify Individuals at Risk of Unfavourable Treatment Outcomes

Manuscript in Preparation: Correlation Between Plasma Cytokine Levels and TB Treatment Outcomes in an Indian Cohort

Aim 2: Markers of treatment response

2A: Identify TB treatment response biomarkers

Proteomic Discovery of Protein-based TB Recurrence and Death Signatures

Aim: To identify protein biomarkers associated with TB recurrence and mortality through high-sensitivity proteomic analysis using mass spectrometry.

Principal Investigators: Sanjeeva Srivastava (IIT-Bombay), Sonia Krishnan (JHU), Amita Gupta (JHU), Mandar Paradkar (BJGMC-JHU CRS), Sanjay Gaikwad (BJGMC), Rajesh Kayakarte (BJGMC), Vandana Kulkarni (BJGMC-JHU CRS)

Status: Study completed

Submitted Manuscript: Plasma Proteomic Signatures Distinguish Treatment Resolution and Recurrence in Tuberculosis Patients- iScience

Comorbidities and Their Impact on Treatment Response

Aim: To assess the influence of undernutrition, diabetes, smoking, and alcohol use on TB treatment outcomes and biomarker performance and explore the feasibility of integrating

Proposed Manuscript: Nutritional and Comorbidity Factors Affecting TB Treatment Outcomes in India

Status: Analysis ongoing

Manuscript Accepted by IJTLD: Ezhumalai K, Rao PS, Babu SP, Jeyakumar SM, Bollinger RC, Gupta A, Sarkar S, Heysell SK, Mave V, Sinha P, Bhavani PK. Impact of Nutritional Status and Diabetes on the Pharmacokinetics of First-Line Anti-TB Drugs among Persons with Pulmonary Tuberculosis in India (Intensive PK).

Manuscript Under Review: Rao NK, Cintron C, Babu SP, Karoly M, Mehta S, Gupte AN, Sivaprakasam A, Bhavani PK, Salgame P, Paradkar M, Gaikwad S, Mave V, Gupte N, Thangakunam B, Christopher DJ, Horsburgh CR, Gupta A, Ellner JJ, Sarkar S, Hochberg N, Viswanathan V, Sinha P. High Prevalence of Micronutrient Deficiency Among Indian Adults with Tuberculosis- IJTLD.

Clinical Treatment Response Prediction

Aim: To develop and evaluate predictive models for TB treatment response that integrate clinical data, RNA signatures, and biomarker-based risk scores, ensuring affordability and feasibility for implementation in Indian clinical settings

Principal Investigators: Sonya Krishnan (JHU), Matthew Robinson (JHU), Amita Gupta (JHU), Bruno Andrade (JHU)

Status: Study completed

Manuscript Under Review at Annals of ATS : Prediction of Individual Unfavorable TB Treatment Outcomes in Brazil and India Using Machine Learning

Aim 2: Markers of treatment response

2B: Investigate host-related mechanisms of treatment failure

Investigate Host-Related Mechanisms of Treatment Failure

1. **Investigate Host-Related Mechanisms of Treatment Failure:** To assess how undernutrition and diabetes mellitus (DM) influence TB treatment outcomes, particularly their impact on drug pharmacokinetics (PK) and pharmacodynamics (PD). This study will investigate whether these comorbidities contribute to lower drug concentrations, leading to treatment failure, recurrence, and drug resistance.

Status: Analysis underway

- **Aim:** Comparison of drug concentrations across different patient groups
Status: Analysis ongoing
- **Aim:** Relationship between body composition changes and treatment outcomes
Status: Analysis ongoing

- **Aim:** To establish preliminary links between TB drug concentrations and clinical outcomes among patients with DM and/or undernutrition

Manuscript accepted by IJTLD: Ezhumalai K, Rao PS, Babu SP, Jeyakumar SM, Bollinger RC, Gupta A, Sarkar A, Heysell SK, Mave V, Sinha P, Bhavani PK. Impact of Nutritional Status and Diabetes on the PK of First-Line Antituberculosis Drugs among Adults with Pulmonary Tuberculosis in India.

2. Influence of gut pathogens and microbiome on drug PK and treatment success

- **Aim:** To determine whether DM and undernutrition significantly alter TB drug pharmacokinetics, necessitating therapeutic drug monitoring or dose adjustments to improve treatment outcomes. Additionally, this study will explore the role of enteropathogens in drug absorption and treatment efficacy, offering insights into potential microbiome-based interventions for TB patients.

Proposed Manuscript: Prevalence of Intestinal Parasitic Co-infections among TB Patients in India

Status: Analysis underway

Aim 3: Investigating the impact of lung injury on TB treatment outcomes

Association Between Lung Injury and Treatment Outcomes

Aim: To measure the association between clinical, functional, and imaging markers of lung injury and unfavorable TB treatment outcomes in newly diagnosed drug-susceptible PTB cases in India.

Principal Investigators: Akshay Gupte (BU), DJ Christopher (CMC)

Proposed Manuscript: Association between Lung Injury Markers and Treatment Response in PTB Cases

Status: Preliminary analysis ongoing

Aim 3: Investigating the impact of lung injury on TB treatment outcomes *Continued*

Identification of Plasma and Sputum Inflammatory Markers

Aim: To identify inflammatory markers in plasma and sputum associated with lung injury in PTB cases.

Principal Investigators: Akshay Gupte (BU), DJ Christopher (CMC)

Proposed Manuscript: Inflammatory Markers of Lung Injury in PTB Cases

Status: Study testing and analyses will be completed by AIRMAIL RO1

Characterization of Lung Injury Phenotypes

Aim: To categorize lung injury phenotypes and their prevalence in successfully treated PTB cases in India

Principal Investigators: Akshay Gupte (BU), DJ Christopher (CMC)

Proposed Manuscript: Characterization of Lung Injury Phenotypes During and After PTB Treatment

Status: Final analysis ongoing

Abstract Accepted ERS 2026: Lung injury in pulmonary TB: functional impact and recovery with treatment- Aim 3 Data. Christopher DJ, Kodali LK, Gaikwad S, Paradkar M, Thangakunam B, Bhavani PK, Aggarwal A, Gupte A on behalf of the RePORT-India TB Research Consortium

Aim: To build on Phase 1 findings, which demonstrated that microbiologically cured PTB patients often exhibit significant lung function impairment. This study will expand the investigation into inflammatory markers, lung function, and imaging to predict treatment outcomes and long-term respiratory health.

Principal Investigators: Akshay Gupte (BU), DJ Christopher (CMC)

Proposed Manuscript: Risk-factors of Lung Injury among Adult PTB Patients in India

Status: Analysis ongoing

Pulmonary Function and Exercise Testing

Aim: To assess lung function impairment using spirometry, 6-minute walk tests (6MWT), and additional lung function assessments (TLC and DLCO) in a subset of participants.

Principal Investigators: Akshay Gupte (BU), DJ Christopher (CMC)

Status: Final analysis ongoing

Abstract Accepted to ERS 2026: Kodali LS, Paradkar M, Thangakunam B, Gaikwad S, Bhavani PK, Aggarwal A, Mave V, Gupta A, Christopher DJ, Gupte AN, on behalf of the RePORT-India TB Research Consortium. GLLI race-neutral versus regional spirometry reference equations for classifying post-tuberculosis lung disease in India Aim 3 Data.

Abstract Accepted to The Union 2026: Kodali LS, Paradkar M, Thangakunam B, Gaikwad S, Bhavani PK, Aggarwal A, Mave V, Gupta A, Christopher DJ, Gupte AN, on behalf of the RePORT-India TB Research Consortium. Establishing Minimal Clinically Important Differences in Lung Function Among Adults with Pulmonary Tuberculosis.

Abstract Accepted to RePORT International Annual Meeting Jr. Investigators 2026: Kodali LS, Paradkar M, Thangakunam B, Gaikwad S, Bhavani PK, Aggarwal A, Mave V, Gupta A, Christopher DJ, Gupte AN, on behalf of the RePORT-India TB Research Consortium. Alcohol Misuse is Associated with Worse Lung Function and Respiratory Health Status in Pulmonary Tuberculosis.

Aim 3: Investigating the impact of lung injury on TB treatment outcomes

Continued

Lung Imaging

Aim: To evaluate lung injury through chest X-ray (CXR), high-resolution CT (HR-CT), and PET-CT scans at multiple time points to assess structural and inflammatory changes in response to TB therapy.

Principal Investigators: Akshay Gupte (BU), DJ Christopher (CMC)

Proposed Manuscript: Evaluation of PET-CT Imaging in Monitoring TB Treatment Response

Status: Ongoing

Proposed Manuscript: Quantitative imaging of TB-associated lung injury

Status: Preliminary analysis ongoing

Respiratory Health Status

Aim: To measure respiratory health outcomes using validated patient-reported assessments (SGRQ, CAT, MMRC) to track quality of life and treatment response.

Status: Preliminary analysis ongoing

Cytokine Testing

Aim: To measure inflammatory cytokine levels in plasma and sputum samples to assess their role in lung injury and treatment response.

Principal Investigators: Akshay Gupte (BU), DJ Christopher (CMC)

Proposed Manuscript: Cytokine Signatures and TB Treatment Outcomes

Status: Study testing and analyses will be completed under AIRMAIL RO1

Sputum Storage for Mtb mRNA

Aim: To store induced sputum samples for future studies correlating residual lung inflammation on PET-CT with Mtb mRNA transcription and TB recurrence.

Treatment Outcomes

Aim: To define unfavorable TB treatment outcomes, including failure, recurrence, death, and emerging drug resistance, aligning with Aim 2 methodologies.

Principal Investigators: Akshay Gupte (BU), DJ Christopher (CMC)

Proposed Manuscript: Impact of Lung Injury on TB Recurrence and Mortality

Status: Preliminary analysis ongoing

Aim 4A: Examine host antimicrobial pathways in inducing their IR phenotype in HHC

Examine Host Antimicrobial Pathways in Inducing the IR Phenotype in HHCs

Aim: To test whether the IR phenotype is characterized by enhanced antimicrobial and IL-17 immune pathways, leading to effective innate resistance against Mtb infection.

Principal Investigator: Padmini Salgame (Rutgers)

Proposed Manuscripts:

- Differential Activation of Innate Immune Pathways in TB-Exposed Individuals
- Role of IL-36 and PGE2 in Mediating TB Resistance: Detailed examination of the IL-36 and PGE2 pathways in macrophage-mediated Mtb control.
- Antigen-Specific Th17 Responses in TB Resistance: Analysis of Th17 cell responses and their contribution to the IR phenotype
- Cytokine Balance and TB Resistance: Analysis of the balance between IL-36, PGE2, IL-1, and type I IFN in TB resistance

Status: Potential studies for future

Aim 5: Progression to disease: identify immunologic markers of persons at highest risk of progression of latent TB infection to TB

Progression to Disease: Identifying Immunologic Markers of Persons at Highest Risk of Progression from Latent TB Infection to Active TB

Aim: To identify immunologic biomarkers that predict which individuals with latent TB infection (LTBI) are at the highest risk of progressing to active TB disease. This will enable targeted preventive therapy, optimizing public health interventions in TB-endemic settings.

Aim 5A: Stored samples: validation of PREDICT29 in progressors & non-progressors from RePORT

Validation of PREDICT29 Biomarker in Progressors & Non-Progressors

Aim: To validate PREDICT29, a novel blood biomarker signature, in RePORT India cohorts for its ability to stratify individuals at risk of TB progression.

Principal Investigator: Padmini Salgame (Rutgers)

Status:

- NanoString based testing of all samples has been completed.
- Additional total RNA seq was performed on PaxGene derived RNA to support cross platform validation.
- Final data integration and manuscript writing are underway.

Aim 5B: Immune & hormone studies in freshly collected samples

Pediatric versus Adult TB Patients

Aim: To understand differences in immune cell profiles and antigen-specific cytokine patterns among children and adults with various forms of ATB.

Principal Investigators: Vijaya Valluri (BMMRC), Prudula Kamakshi (BMMRC), Krishna Vankayalapati (SLU)

Status: Manuscript is complete and currently being revised by the PIs. It will be communicated shortly. Data from this study will be presented during this year's young investigators session.

T-Regulatory Cell Function

Aim: To evaluate the suppressive function of CD4⁺CD25⁺FoxP3⁺ Tregs and their association with TB progression.

Principal Investigators: Vijaya Valluri (BMMRC), Prudula Kamakshi (BMMRC), Krishna Vankayalapati (SLU)

Status: This data will be included in the manuscript mentioned in Developing an ELISA-Based Kit for TB Progression Prediction study

Signaling Pathways & MicroRNA Regulation

Aim: To identify signaling molecules and microRNAs that regulate immune responses in TB progressors versus non-progressors.

Principal Investigators: Vijaya Valluri (BMMRC), Prudula Kamakshi (BMMRC), Krishna Vankayalapati (SLU)

Proposed Manuscript: MicroRNA-1246 regulates macrophage lipid metabolism and is involved in resistance to human Mycobacterium tuberculosis infection.

Status: Manuscript currently under revision after submission to PLOS Pathogens.

Developing an ELISA-Based Kit for TB Progression Prediction

Aim: To develop a multiplex ELISA kit for detecting early immunologic markers of TB progression, similar to QuantiFERON-TB Gold Plus.

Principal Investigators: Vijaya Valluri (BMMRC), Prudula Kamakshi (BMMRC), Krishna Vankayalapati (SLU)

Proposed Manuscript: Development and Validation of a Diagnostic Kit for Early TB Risk Detection: Analyze the cytokine and chemokine production capacity of these cells.

Status: Samples being analyzed; follow-ups ongoing

Identifying Immune Biomarkers in Children Who Never Develop TB infection or Disease

Aim: To understand why some children never develop LTBI/ATB using flow cytometry, hormone analysis, and RNA sequencing data.

Status: Manuscript complete and under revision. It will be communicated shortly. Part of this data was presented in previous meetings (2024) during the junior investigators' session. Many additional experiments followed.

Aim 5B: Immune & hormone studies in freshly collected samples

Continued

Identify Immune Differences in HIV Positive Children Compared with Healthy Children

Status: Manuscript under revision with Frontiers in Immunology. Part of this data was previously presented during the junior investigators' session (2023).

Title: Defective IL-17 production leads to reduced IL-1 β levels in response to Mycobacterium tuberculosis in HIV+ children with latent tuberculosis infection.

Epidemiology Studies

Predictors of Poor TB Treatment Outcomes

Proposed Manuscript: Identifying Predictors of Poor TB Treatment Outcomes in the Context of Comorbidities and Healthcare Settings

Status: Ongoing

Publication: Prakash Babu S, Ezhumalai K, Raghupathy K, Karoly M, Chinnakali P, Gupte N, Paradkar M, Devarajan A, Dhanasekaran M, Thiruvengadam K, Dauphinais MR. Factors associated with unfavorable treatment outcomes among persons with pulmonary tuberculosis: A multicentric prospective cohort study from India. Clinical Infectious Diseases. 2024 Oct 15;79(4):1034-8.

Studying Gender-related Differences in TB Disease Presentation and Outcomes

Proposed Manuscript: Gender Disparities in TB Disease Presentation and Outcomes

Status: Data being analyzed with RICC data

Validating the Diagnostic Algorithm for Pediatric TB Suspects

Proposed Manuscript: Validating a Diagnostic Algorithm for Pediatric TB Suspects

Status: Idea for future study

Describing Causes of Death and Associated Risk Factors in TB Patients During and After Therapy

Proposed Manuscript: Mortality in TB Patients: Causes and Risk Factors During and Post-Therapy

Status: Idea for future study

Assessing the Burden of TB Disease and Infection at the Household Level

Proposed Manuscript: Household Clustering of TB Disease and Infection: An Assessment of Community Burden

Status: Ongoing

Epidemiology Studies

Continued

Assessing the Burden of TB Disease and Infection at the Household Level

Proposed Manuscript: Household Clustering of TB Disease and Infection: An Assessment of Community Burden

Status: Ongoing

Identifying Characteristics Associated with Prevalent and Incident TB Disease in Households

Proposed Manuscript: Patient Characteristics, Including Comorbidities, Associated with Tuberculosis among Presumptive TB Patients in India

Status: Data analysis complete. Findings are being compiled, and manuscript is currently under preparation for submission to a peer-reviewed journal.

Identifying Characteristics Associated with TST/QFT Discordance

Proposed Manuscript: Factors Contributing to TST/QFT Discordance in Household TB Contacts

Status: Manuscript outline under preparation (Part of the RePORT India 2025 Writing Workshop)

NIRT-ICER





PUBLICATIONS

MVDRC



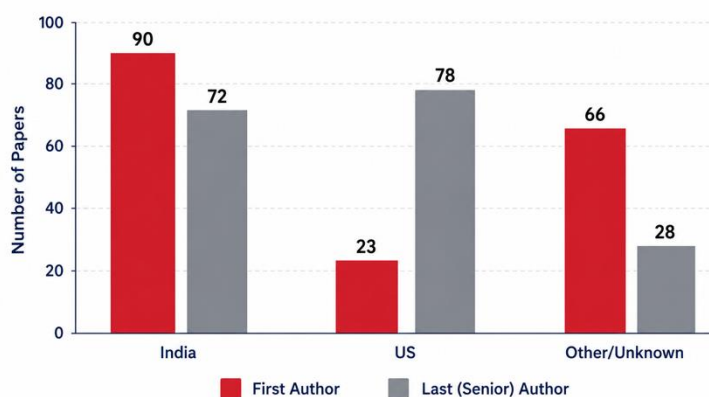
187 Papers published since 2015



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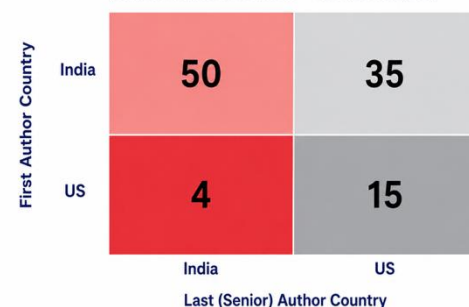
RePORT India Publications:

Authorship Country (First vs Last)

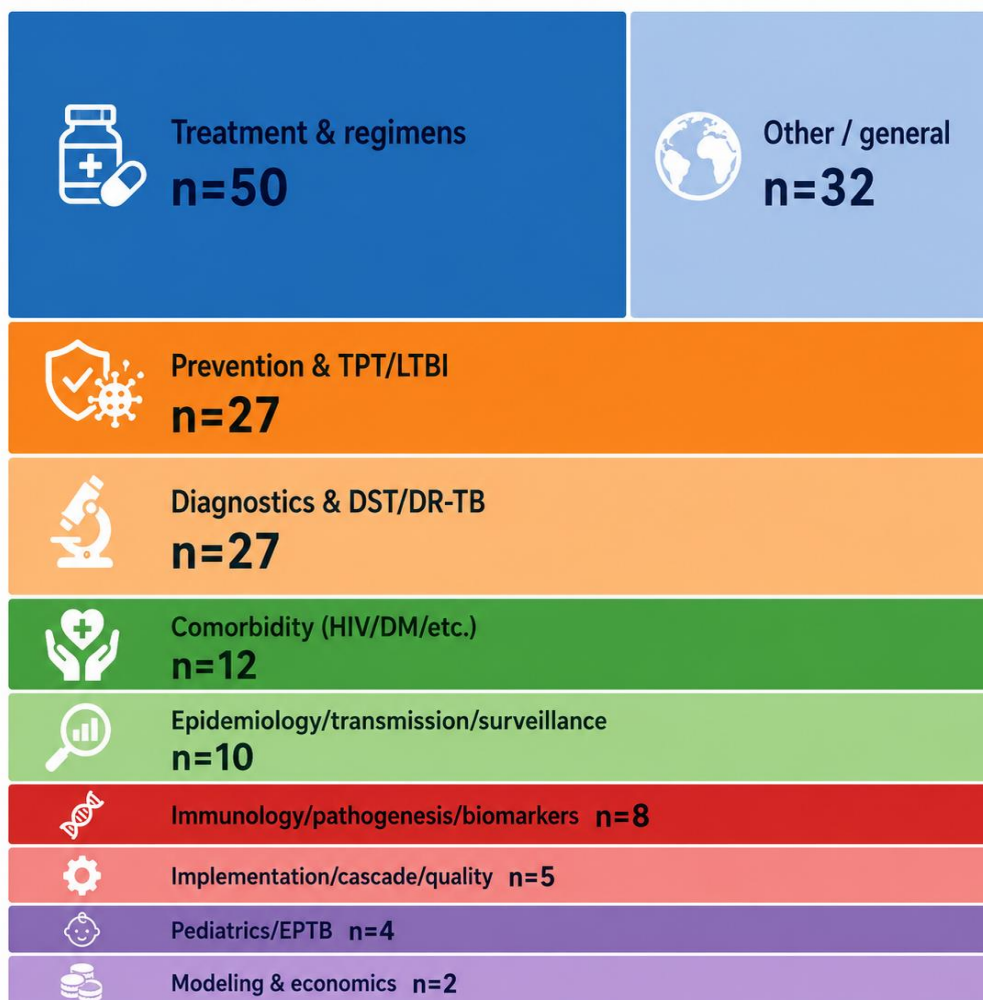


India vs US Authorship

(Subset where both first + last are India/US)



Topic Treemap (Keyword-based) — RePORT India Publications



Accepted Publications

Impact of Nutritional Status and Diabetes on the PK of First-Line Antituberculosis Drugs among Adults with Pulmonary Tuberculosis in India- *IJTLD*

Asymptomatic and symptomatic recurrence of tuberculosis among cured pulmonary tuberculosis patients in India- *IJTLD*

Detection and determinants of asymptomatic recurrence of tuberculosis among cured pulmonary tuberculosis patients in India- *IJTLD*

Analytical method development and validation for clofazimine in human plasma and application of LC-MS/MS based methods for clofazimine and bedaquiline in Indian MDR-TB patients stratified by HIV coinfection- *Journal of Mass Spectrometry*.

2026

A multi-omics study reveals pathway-level insights and predictive biomarkers in pediatric TB

Mousavian Z, Segal MR, Calderon RI, Luiz J, Nkereuwem E, Wambi P, Paradkar M, Franke MF, Källénus G, Kampmann B, Kinikar A, Sigal GB, Sundling C, Swaney DL, Wobudeya E, Zar HJ, Collins JM, Cattamanchi A, Ernst JD, Jaganath D. A multi-omics study reveals pathway-level insights and predictive biomarkers in pediatric TB. *Clin Proteomics*. 2026 Jun 8;23(1):31. doi: 10.1186/s12014-026-09614-3. PMID: 42260364; PMCID: PMC13277094.

Pulmonary Tuberculosis Detection with MiniDock MTB Using Swab Samples

Yerlikaya S, Chirwa M, Ajide B, Castro MDM, Ha H, Kato-Maeda M, Kisakye E, Marcelo D, Mochizuki T, Rockman L, Steadman A, Thangakunam B, Bimba JS, Christopher DJ, Muyoyeta M, Phan H, Theron G, Yu C, Kremer K, Phillips PPJ, Nahid P, Denking CM, Cattamanchi A, Andama A; R2D2 TB Network and SMART4TB Consortia. *N Engl J Med*. 2026 Apr 30;394(17):1710-1722. doi: 10.1056/NEJMoa2509761. PMID: 42054680; PMCID: PMC13132025.

Use of dried plasma spots to monitor rifampicin concentrations in resource-constrained settings

Santhosh S, Aruldas BW, Christopher DJ, Prabha R, Thangagunam B, Mathew BS. *Int J Tuberc Lung Dis*. 2026 Mar 27;30(4):174-179. doi: 10.5588/ijtld.25.0332. PMID: 41896718.

Novel Genetic Locus Associated with Resistance to *M. tuberculosis* Infection: A Multi-Ancestry Genome-Wide Association Study

Gandhi NR, Fernandes Gyorfy M, Paradkar M, Jennet Mofokeng N, Figueiredo MC, Prakash S, Prudhula Devalraju K, Hui Q, Willis F, Mave V, Andrade BB, Moloantoa T, Kumar Neela VS, Campbell A, Liu C, Young A, Cordeiro-Dos-Santos M, Gaikwad S, Karyakarte R, Rolla VC, Kritski AL, Collins JM, Shah NS, Brust JCM, Valluri VL, Sarkar S, Sterling TR, Martinson NA, Gupta A, Sun YV. *medRxiv [Preprint]*. 2026 Mar 7:2026.03.06.26347614. doi: 10.64898/2026.03.06.26347614. PMID: 41867181; PMCID: PMC13004093.

Complement profiling for treatment outcomes in pulmonary TB

Pavan Kumar N, Nancy P A, Hissar S, Sivakumar S, Viswanathan V, Bethunaickan R, Kornfeld H, Babu S. *Front Immunol*. 2026 Feb 11;17:1679947. doi: 10.3389/fimmu.2026.1679947. PMID: 41756295; PMCID: PMC12932523.

Application of a Liquid Chromatography: Tandem Mass Spectrometry Based Method to Determine Plasma Cycloserine Concentrations in Indian MDR-TB Patients—A Pilot Study

Lokhande RV, Arora PR, Rodrigues C, Bhagure GR, Udawadia ZF, Gupta A, Tornheim JA, Ashavaid TF, Pinto LM, Mullerpattan JB, Sunavala A, Patel J, Dherai AJ, Thakur S, Pandya H, Sawant N, Joubert A, Wiesner L, Martinson NA; Indo-South Africa Study T. *Indian J Clin Biochem*. 2026 Feb 2. doi:10.1007/s12291-026-01390-z.

*2026 Continued***Application of a Liquid Chromatography: Tandem Mass Spectrometry Based Method to Determine Plasma Cycloserine Concentrations in Indian MDR-TB Patients—A Pilot Study**

Lokhande RV, Arora PR, Rodrigues C, Bhagure GR, Udwardia ZF, Gupta A, Tornheim JA, Ashavaid TF, Pinto LM, Mullerpattan JB, Sunavala A, Patel J, Dherai AJ, Thakur S, Pandya H, Sawant N, Joubert A, Wiesner L, Martinson NA; Indo-South Africa Study T. Indian J Clin Biochem. 2026 Feb 2. doi:10.1007/s12291-026-01390-z.

Multicohort assessment of plasma metabolic signatures of tuberculosis disease in children: a retrospective cross-sectional study

Nellis MM, Luiz J, Jaganath D, Mousavian Z, Nkereuwem E, Wambi P, Calderon R, Paradkar M, Castro R, Nerurkar R, Franke MF, Kinikar A, Wobudeya E, Zar HJ, Jones DP, Segal M, Sigal G, Swaney DL, Cattamanchi A, Ernst JD, Ziegler TR, Kampmann B, Collins JM; COMBO Study. Sci Rep. 2026 Jan 23;16(1):3283. doi: 10.1038/s41598-025-32679-3. PMID: 41577684; PMCID: PMC12835163.

Catalysing Artificial Intelligence for Paediatric Tuberculosis Research (CAPTURE): protocol for a global multicentre study establishing a paediatric chest X-ray repository to evaluate computer-aided detection algorithms

Palmer M, Kik SV, Kohli M, Fataar A, Anyebe V, Frey N, Castro R, Nerurkar R, van der Westhuizen JN, Macé A, Ruhwald M, Seddon JA, Jaganath D; CAPTURE Consortium group. BMJ Open. 2026 Jan 12;16(1):e108668. doi: 10.1136/bmjopen-2025-108668. PMID: 41526020; PMCID: PMC12815126.

Contribution of Key Comorbidities to Unfavorable Treatment Outcomes Among Adults With Drug-Sensitive Pulmonary TB in India: A Prospective Cohort Analysis

Sinha P, Karoly M, Padmapriyadarsini C, Paradkar M, Mave V, Gupte N, Gupta A, Dauphinais M, Babu SP, Gaikwad S, Cox SR, Golub J, Cintron C, Thangakunam B, Ezhumalai K, Ponnuraja C, Tornheim JA, Christopher DJ, Viswanathan V, Ellner JJ, Kornfeld H, Horsburgh CR Jr, Shivakumar SVBY, Salgame P, Bollinger RC, Sarkar S, Gupte AN; RePORT-India TB Research Consortium. Chest. 2026 Jan;169(1):64-72. doi: 10.1016/j.chest.2025.05.055. Epub 2025 Sep 10. PMID: 40939932; PMCID: PMC13169425.

*2025***Quantitation of Plasma Bedaquiline Concentrations in Indian MDR-TB Patients Using Liquid Chromatography-Tandem Mass Spectrometry**

Lokhande RV, Arora PR, Joubert A, Bhagure GR, Udwardia ZF, Gupta A, Rodrigues C, Tornheim JA, Wiesner L, Ashavaid TF; MDR-TB MUKT and RePORT India Study Team; Indo-South Africa Study Team. Biomed Chromatogr. 2025 Dec;39(12):e70243. doi: 10.1002/bmc.70243. PMID: 41235782.

Diagnostic accuracy of swab-based molecular tests for tuberculosis using near-point-of-care platforms: a multi-country evaluation

Steadman A, Kumar KM, Asege L, Kato-Maeda M, Mukwatamundu J, Shah K, Trang T, Ball A, Khimani K, Kim Dung DT, Michael JS, Christopher DJ, Phan H, Yerlikaya S, Nahid P, Denkinger CM, Cattamanchi A, Andama A. EBioMedicine. 2025 Nov;121:105991. doi: 10.1016/j.ebiom.2025.105991. Epub 2025 Oct 31. PMID: 41175672; PMCID: PMC12617638.

Prevalence of Latent Tuberculosis Infection among Spouses and First-Degree Relatives of Pulmonary Tuberculosis Cases in South India

Ezhumalai K, Narasimhan PB, Raghupathy K, Rajan B, Narayanan A, Babu SP, Salgame P, Roy G, Ellner J, Sarkar S. Indian J Public Health. 2025 Oct 1;69(4):508-513. doi: 10.4103/ijph.ijph_115_24. Epub 2025 Oct 8. PMID: 41059942.

2025 Continued

Evaluation of cycloserine dose regimens in an Indian cohort with multidrug-resistant tuberculosis: a population pharmacokinetic analysis

Resendiz-Galvan JE, Arora PR, Lokhande RV, Udwadia ZF, Rodrigues C, Gupta A, Tornheim JA, Denti P, Ashavaid TF; The MDR-TB MUKT and Indo-South Africa Study Teams; MDR-TB MUKT and Indo-South Africa Study Teams.. *Antimicrob Agents Chemother*. 2025 Oct;69(10):e0010125. doi: 10.1128/aac.00101-25. Epub 2025 Sep 2. PMID: 40891988; PMCID: PMC12486832.

TB stigma in India: A narrative review of types of stigma, gender differences, and potential interventions

Carwile ME, Prakash Babu S, Cintron C, Dauphinais M, Pan SJ, Thulasingham M, Horsburgh CR Jr, Sarkar S, Hochberg NS, Sabin LL, Flynn D, Kumar B, Sinha P, Singh UB. *PLOS Glob Public Health*. 2025 Sep 22;5(9):e0005109. doi: 10.1371/journal.pgph.0005109. PMID: 40982550; PMCID: PMC12453202.

Lung and abdominal ultrasound accuracy for tuberculosis: An Indian prospective cohort study

Weber SF, Wolf R, Manten K, Thangakunam B, Isaac B, Shankar D, Mangal D, Dutta AK, Vimala LR, Irodi A, Tobian F, Koeppl L, Beck JS, Wolf P, Bélard S, Denking CM, Christopher DJ; ALL POCUS TB India study group. *PLoS One*. 2025 Sep 3;20(9):e0329670. doi: 10.1371/journal.pone.0329670. PMID: 40901833; PMCID: PMC12407472.

Research Driving Evidence, Practice, and Policy in Tuberculosis (2017–2026)

High Impact	Policy Influence	Scientific Innovation	Global Relevance	Translational Impact
 Published in Leading Journal	 Informing National & Global TB Policies	 Novel Diagnostics, Biomarkers, & Multi-omics Insights	 Studies Across India & Other High TB Burden Countries	 Changing Clinical Practice & Improving TB Outcomes
 	Pulmonary Tuberculosis Detection with MiniDock MTB Using Swab Samples Yerlikaya S, et al (2026) Journal: <i>New England Journal of Medicine</i> Scientific Contributions: Landmark non-sputum TB diagnostic study with strong potential to influence global diagnostic guidelines and implementation.			
 	Impact of Undernutrition on Tuberculosis Treatment Outcomes in India Sinha P, et al (2023) Journal: <i>Clinical Infectious Diseases</i> Scientific Contributions: Landmark prospective multicentre study demonstrating the effect of undernutrition on treatment outcomes; highly relevant for TB nutrition policy.			
 	Undernourished Household Contacts Are at Increased Risk of Tuberculosis Disease, but not TB Infection Sinha P, et al (2024) Journal: <i>Clinical Infectious Diseases</i> Scientific Contributions: First prospective multicentre evidence supporting nutritional interventions for TB contacts; important for preventive strategies.			
 	Factors Associated With Unfavorable Treatment Outcomes among Persons with Pulmonary Tuberculosis: A Multicentric Prospective Cohort Study from India Babu SP, et al (2024) Journal: <i>Clinical Infectious Diseases</i> Scientific Contributions: One of the largest prospective Indian cohort studies identifying risk factors for poor treatment outcomes; directly relevant to NTEP risk stratification.			
 	Contribution of Key Comorbidities to Unfavorable Treatment Outcomes among Adults with Drug-sensitive Pulmonary TB in India Sinha P, et al (2025) Journal: <i>CHEST</i> Scientific Contributions: Demonstrates the importance of diabetes, malnutrition, and other comorbidities; supports integrated patient management.			
 	Predictive Performance of Interferon-Gamma Release Assays and the Tuberculin Skin Test for Incident Tuberculosis Hamada Y, et al. (2023) Journal: <i>EclinicalMedicine</i> Scientific Contributions: International individual participant data meta-analysis informing global preventive therapy and screening strategies.			
	Tuberculosis Preventive Treatment Should Be Considered for All Household Contacts of Pulmonary TB Patients in India Paradkar M, et al (2020) Journal: <i>PLOS ONE</i> Scientific Contributions: Influential evidence supporting expansion of TB preventive treatment for household contacts in India.			
 	QuantIFERON Supernatant-Based Host Biomarkers Predicting Progression to Active Tuberculosis Disease among Household Contacts Daniel EA, et al. (2023) Journal: <i>Clinical Infectious Diseases</i> Scientific Contributions: One of the earliest longitudinal biomarker studies predicting progression from infection to disease; showcases RePORT India's longitudinal cohort.			
 	Predictive Markers of Incident Tuberculosis in Close Contacts in Brazil and India Nogueira BMF, et al. (2025) Journal: <i>Journal of Infectious Diseases</i> Scientific Contributions: International validation of predictive biomarkers across continents; advances precision prevention.			
 	Host Lipidome Predicts Tuberculosis Treatment Failure Shivakoti R, et al. (2022) Journal: <i>European Respiratory Journal</i> Scientific Contributions: High-impact multi-omics study identifying lipid biomarkers predictive of treatment failure; strong translational potential.			
 	Baseline IL-6 is a Biomarker for Unfavorable Tuberculosis Treatment Outcomes: A Multi-site Discovery and Validation Study Gupta AN, et al. (2022) Journal: <i>European Respiratory Journal</i> Scientific Contributions: Large international validation of IL-6 as a prognostic biomarker, supporting risk-based treatment monitoring.			
 	Early Microbiologic Markers of Pulmonary Tuberculosis Treatment Outcomes Paradkar MS, et al. (2023) Journal: <i>Annals of the American Thoracic Society</i> Scientific Contributions: Important for identifying early predictors of treatment success and failure, enabling adaptive patient management.			
 	Diagnostic Accuracy of Swab-Based Molecular Tests for Tuberculosis Using Near-Point-of-Care Platforms: A Multi-Country Evaluation Steadman A, et al. (2025) Journal: <i>eBioMedicine</i> Scientific Contributions: Demonstrates the feasibility of simplified, non-invasive molecular diagnostics across multiple countries.			
 	Food for Thought: Addressing Undernutrition to End TB Sinha P, et al. (2020) Journal: <i>Lancet Infectious Diseases</i> Scientific Contributions: Influential perspective highlighting nutrition as a central pillar of TB elimination; widely relevant to policy discussions.			
 	Drug Resistance and Epidemiological Success of Modern <i>Mycobacterium tuberculosis</i> Lineages in Western India Dixit A, et al. (2024) Journal: <i>Journal of Infectious Diseases</i> Scientific Contributions: Provides important genomic epidemiology data relevant to TB transmission, surveillance, and drug resistance control.			

Key themes

Together, these publications establish RePORT India as a TB leader in:

- TB diagnostics
- Nutrition and TB
- Treatment outcome prediction
- Host biomarkers and multi-omics
- Preventive therapy and household contact research
- Genomic epidemiology and drug resistance

Impact

-  Influencing National (NTEP) & Global (WHO) TB Policies and Guidelines
-  Improving TB Diagnosis, Prevention and Patient Outcomes
-  Building a Strong Evidence Base for End TB Goals
-  Strengthening India's Leadership in TB Research and Innovation

NEIGRIHMS



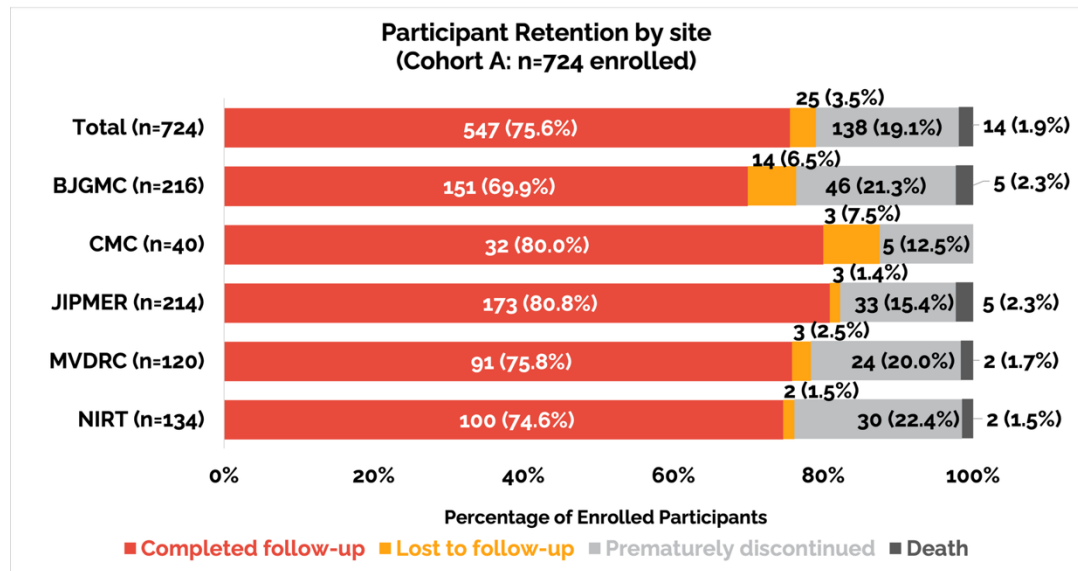
RePCORT

INDIA

DATA

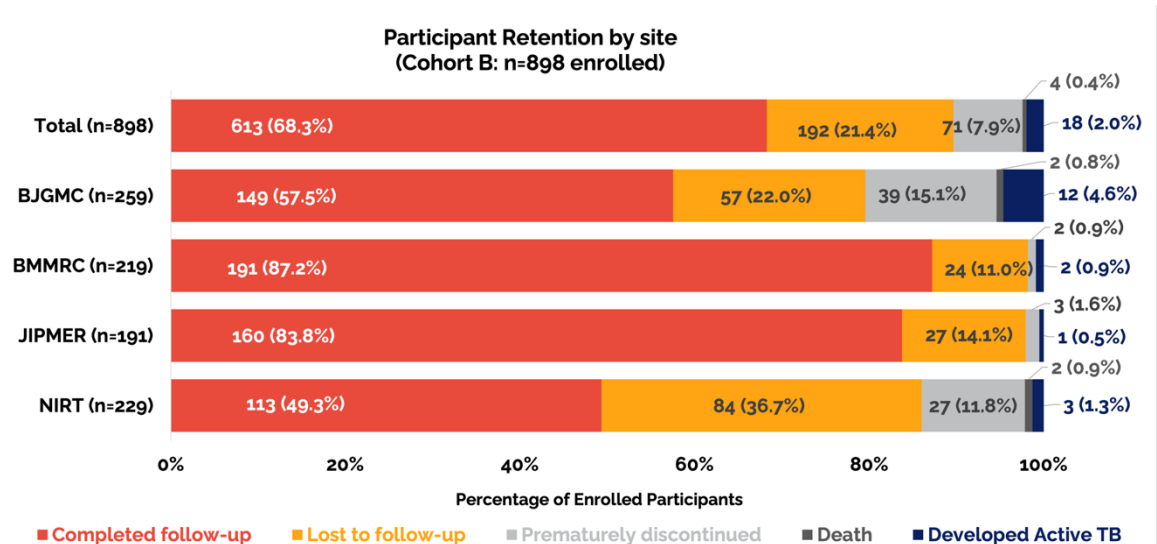
Phase 1: Common Protocol Cohort A: Accrual

	BJGMC	CMC	JIPMER	MVDRC	NIRT	TOTAL
Completed Follow Up	151	32	173	91	100	547
Lost to Follow Up	14	3	3	3	2	25
Prematurely Discontinued	46	5	33	24	30	138
Death	5	0	5	2	2	14
Sum of Enrolled	216	40	214	120	134	724



Phase 1: Common Protocol Cohort B: Accrual

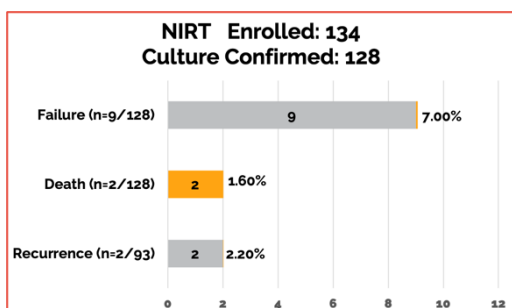
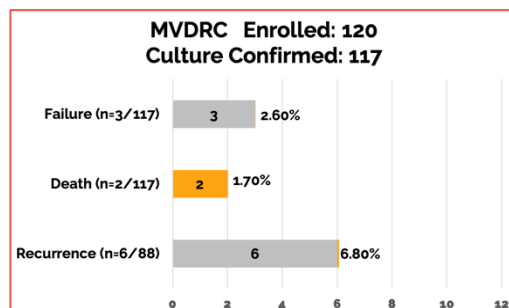
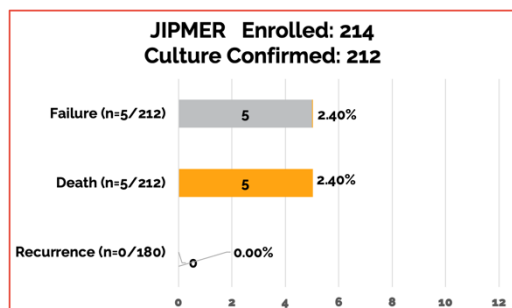
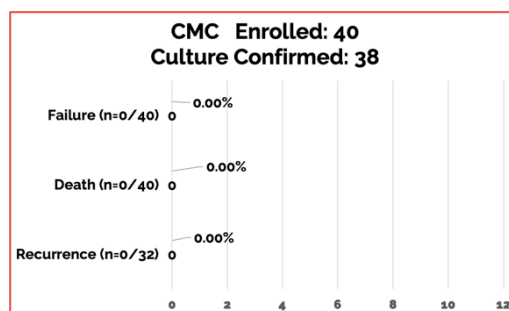
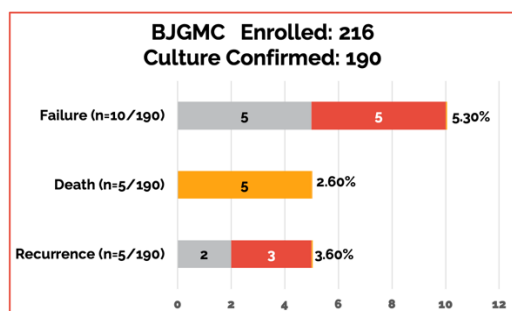
	BJGMC	BMMRC	JIPMER	NIRT	TOTAL
Completed Follow Up	149	191	160	113	613
Lost to Follow Up	57	24	27	84	192
Prematurely Discontinued	39	2	3	27	71
Developed Active TB	12	2	1	3	18
Death	2	0	0	2	4
Sum of Enrolled	259	219	191	229	898



PHASE 1 DATA

Phase 1: Cohort A Treatment Outcomes

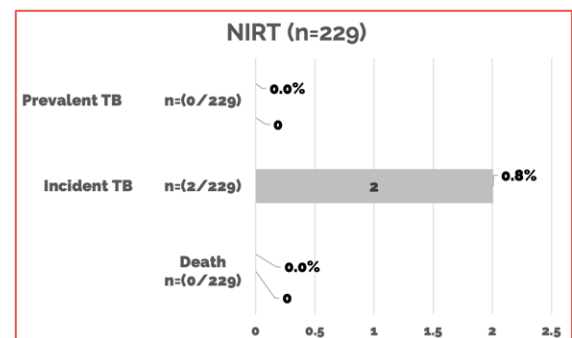
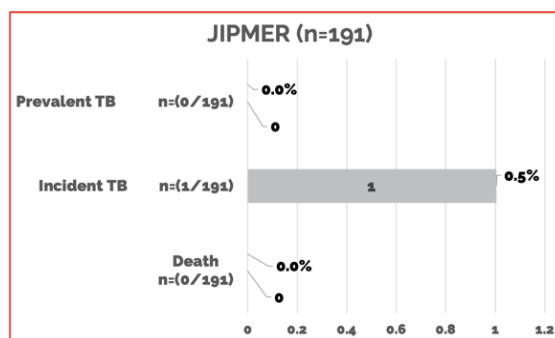
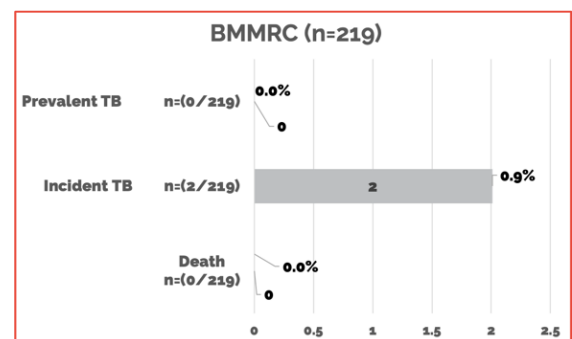
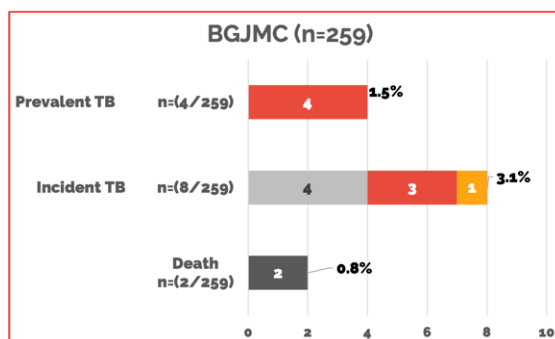
	BJGMC PTB	BGJMC Adult	BJGM C Ped	CMC PTB	JIPMER PTB	MVDRC PTB	NIRT PTB
Enrolled	216	209	7	40	214	120	134
Bacteriologic cure	124	119	5	32	173	88	99
Bacteriologic status indeterminant (Tx complete)	13	13	0	0	0	0	1
Clinical response	2	1	1				
Emerging resistance	2	2	0	0	2	5	0
Bacteriologic failure	5	5	0	0	5	3	9
Clinical failure	5	5	0	0	0	0	0
Treatment incomplete	9	9	0	1	8	1	9
Death	5	5	0	0	5	2	2
Lost to follow up	46	45	1	7	19	11	5
Bacteriological relapse	2	2	0	0	0	6	2
Clinical relapse	3	3	0	0	0	0	0



Bacteriological
Clinical
Total
Death

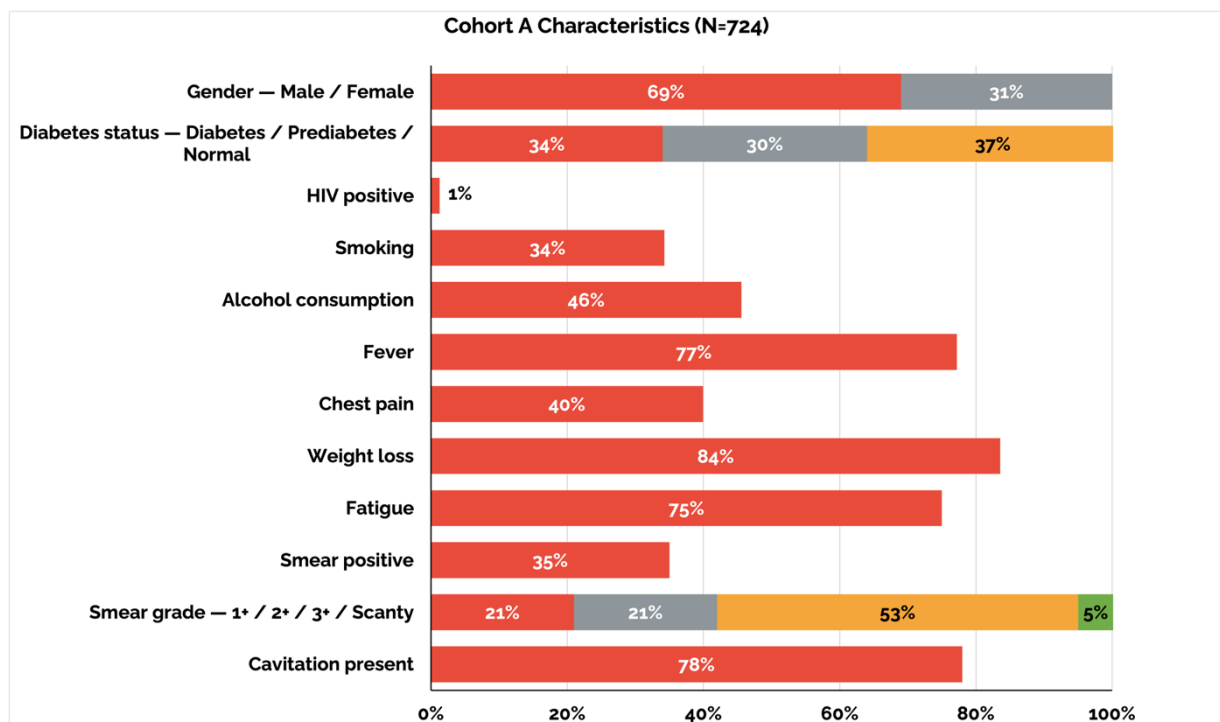
Phase 1: Cohort B Study Outcomes

	BJGMC	BMMRC	JIPMER	NIRT	TOTAL
Enrolled	259	219	191	229	898
No TB	184	202	161	141	688
Prevalent TB (Definite Case)	0	0	0	2	2
Prevalent TB (Probable Case)	4	0	0	0	4
Prevalent TB (Possible Case)	0	0	0	0	0
Incident TB (Definite Case)	4	2	1	2	9
Incident TB (Probable Case)	3	0	0	0	3
Incident TB (Possible Case)	1	0	0	0	1
Death	2	0	0	2	4

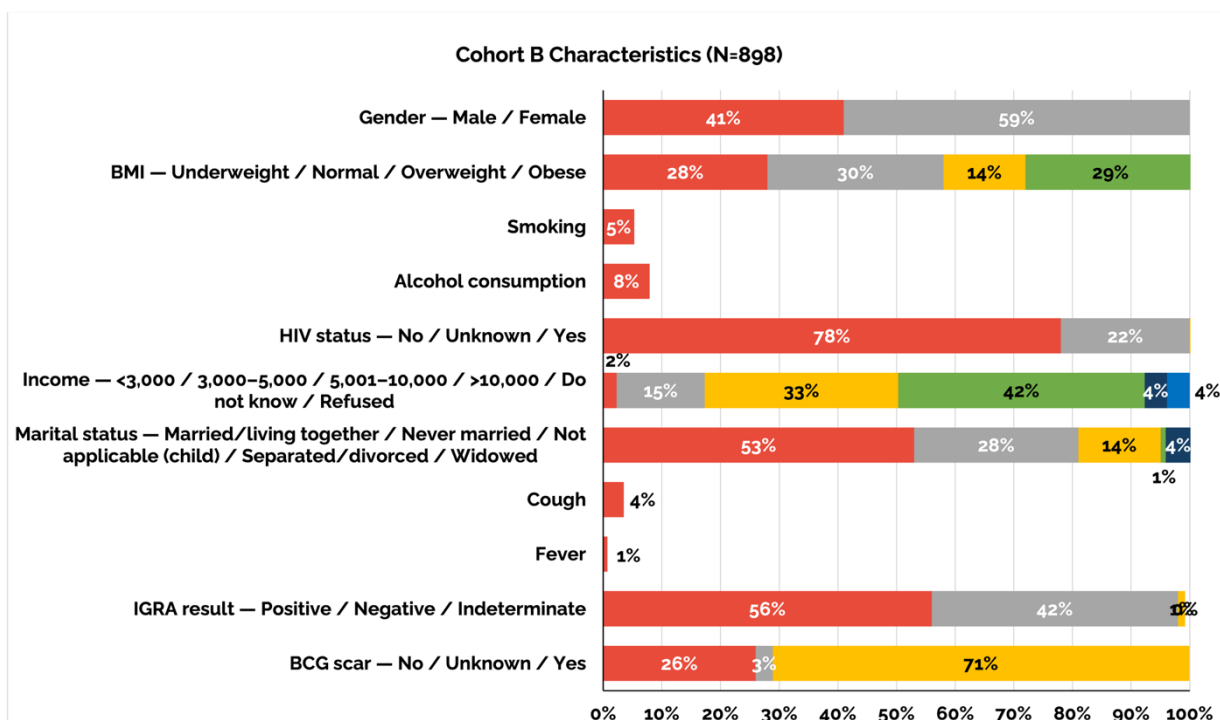


Bacteriological
Clinical
Total
Death

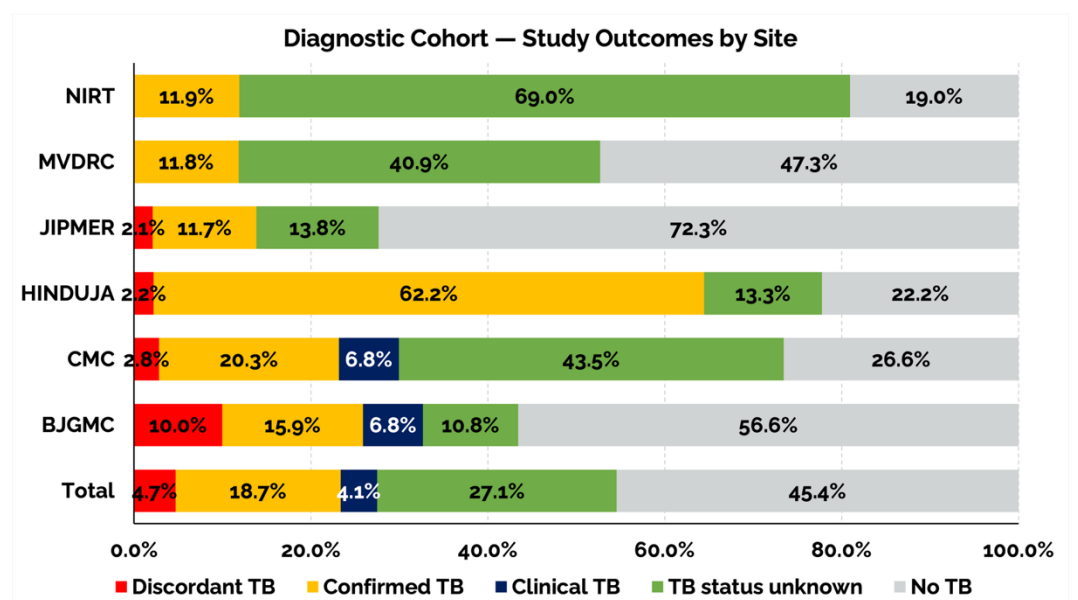
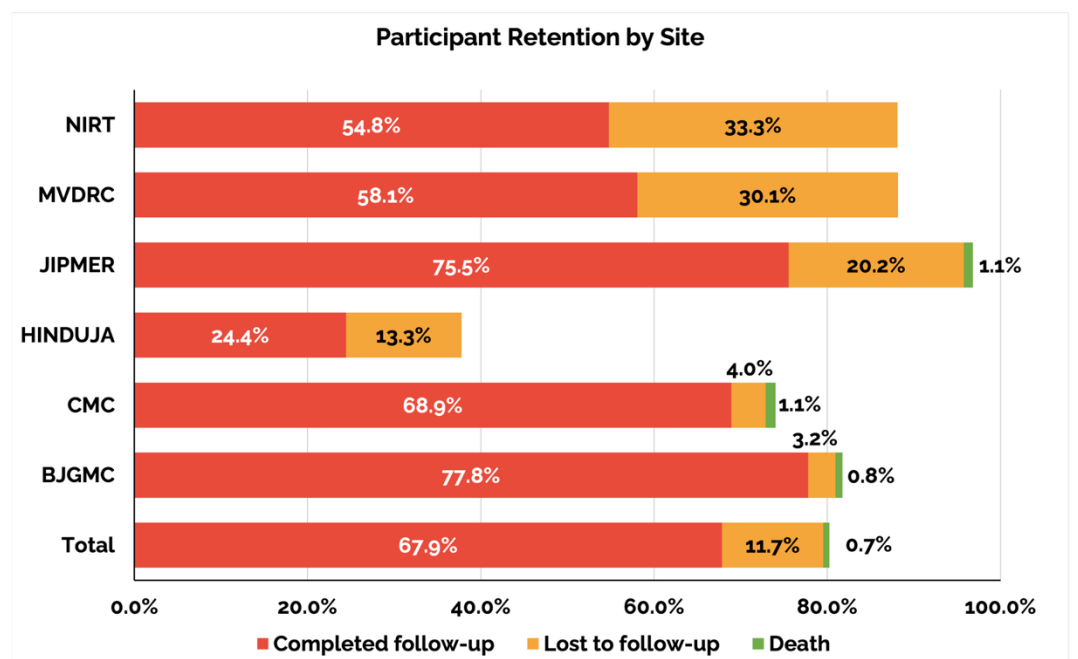
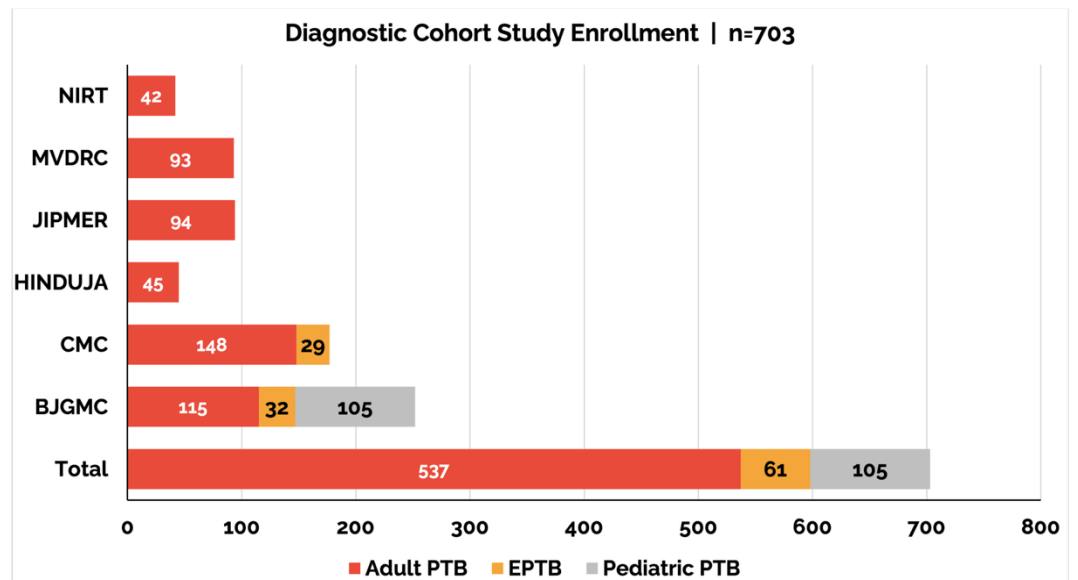
Phase 1: Common Protocol Cohort A: Characteristics



Phase 1: Common Protocol Cohort B: Characteristics

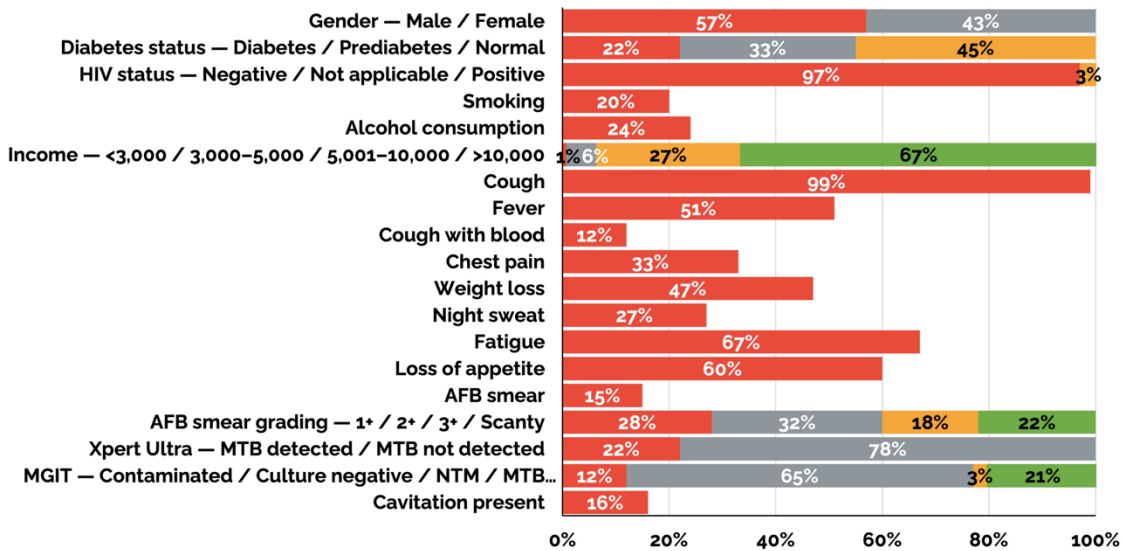


Diagnostic Cohort Enrollment, Retention, & Outcomes

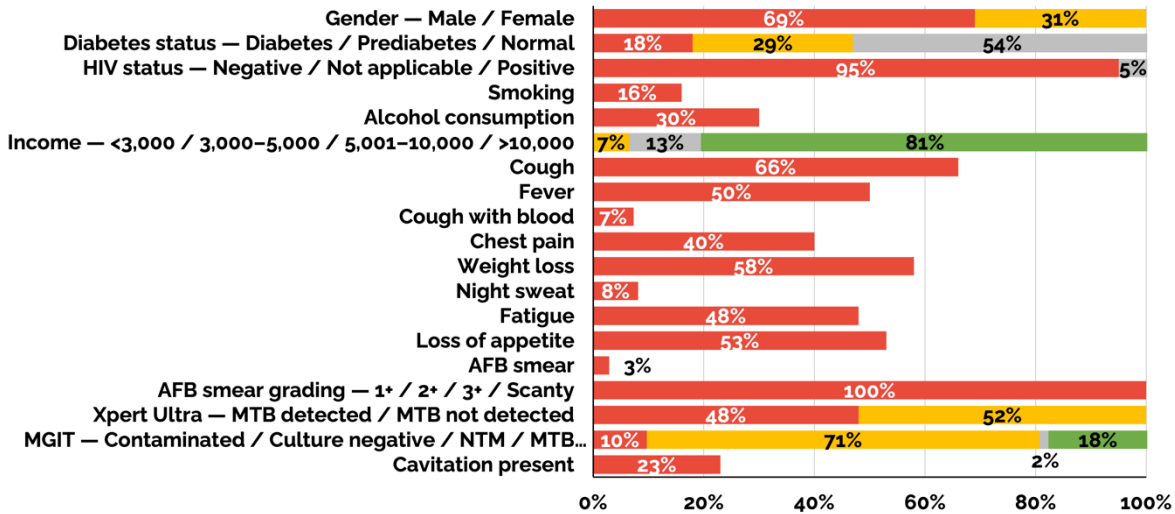


Diagnostic Cohort Characteristics

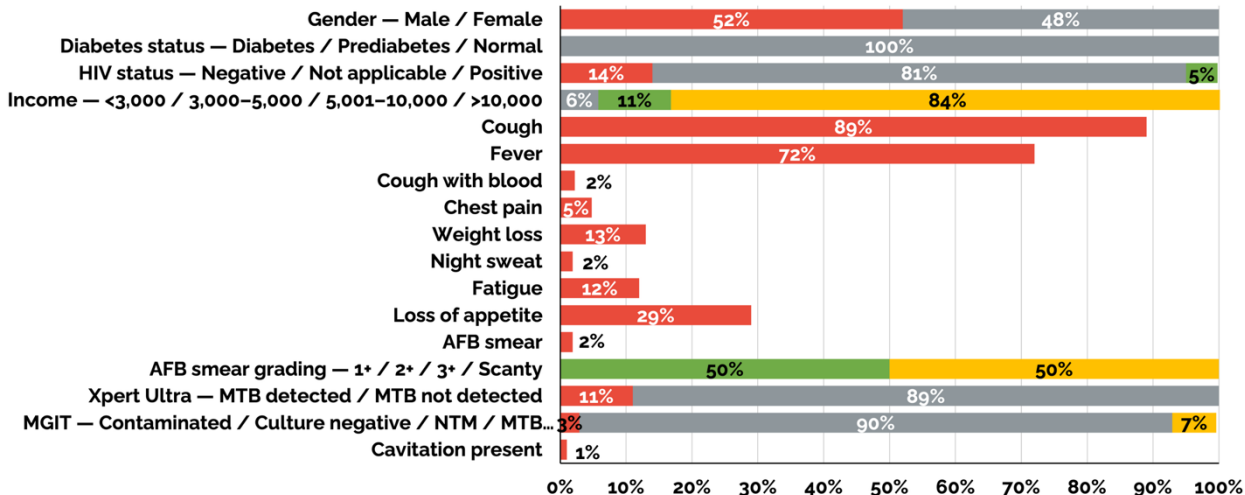
Diagnostic Cohort — PTB Characteristics (N=537)



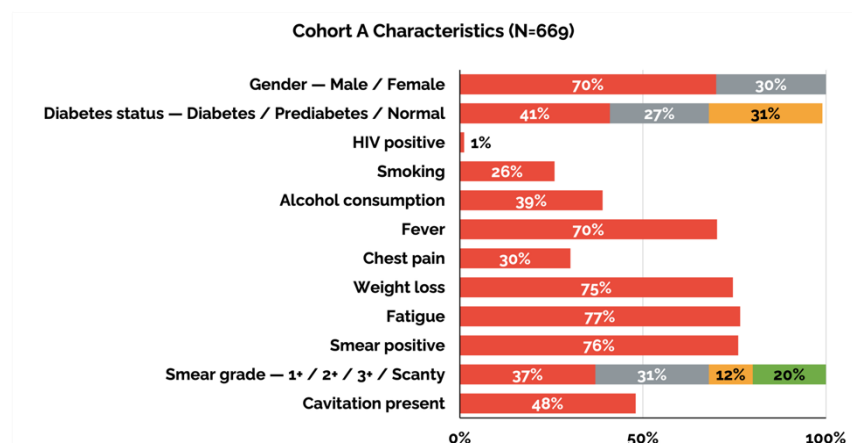
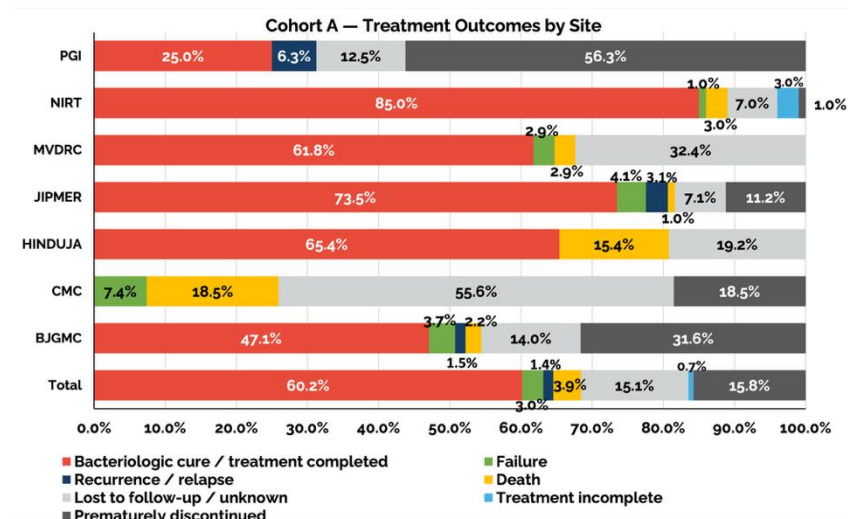
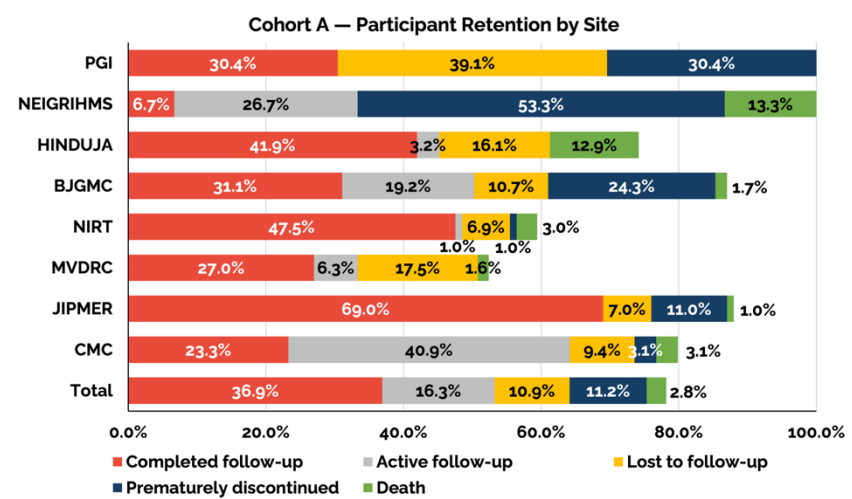
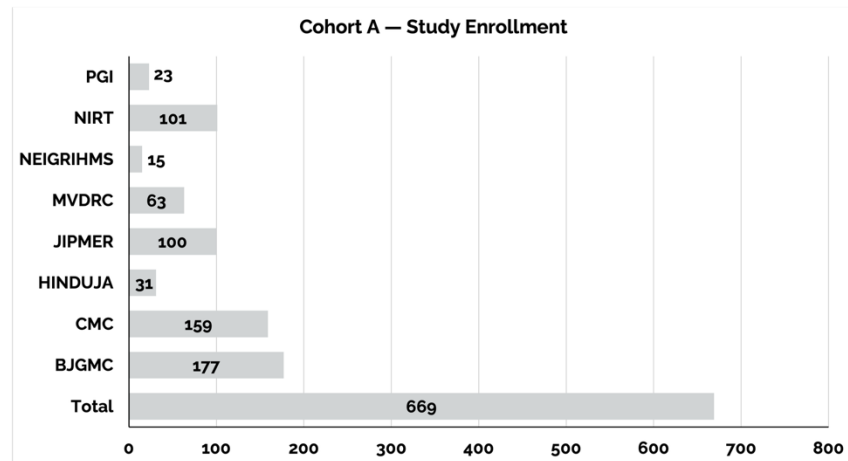
Diagnostic Cohort — EPTB Characteristics (N=62)



Diagnostic Cohort — Pediatric PTB Characteristics (N=104)

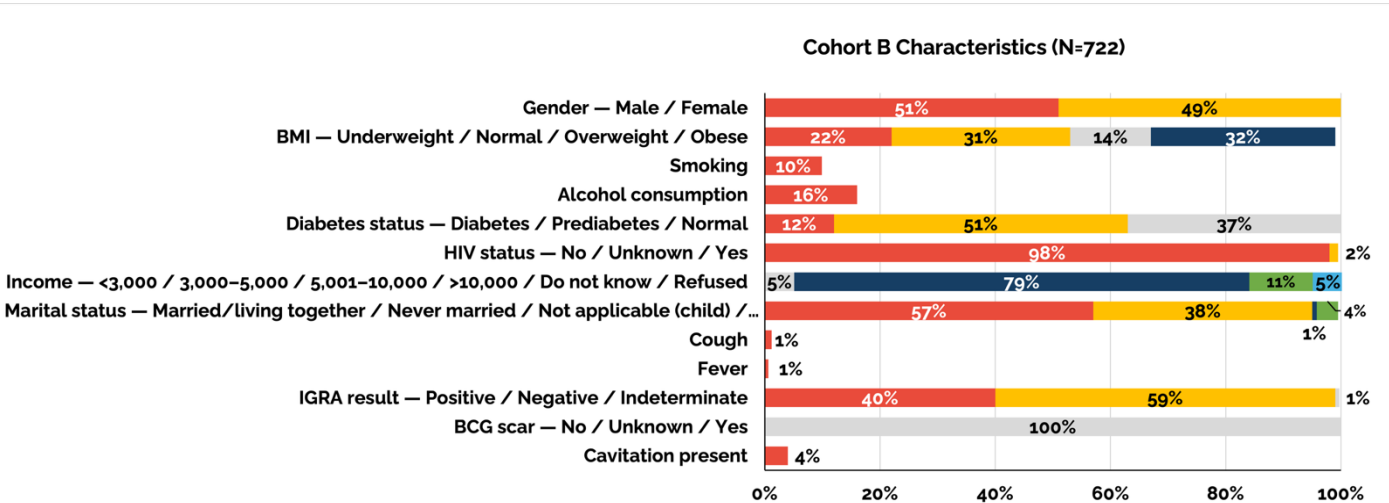
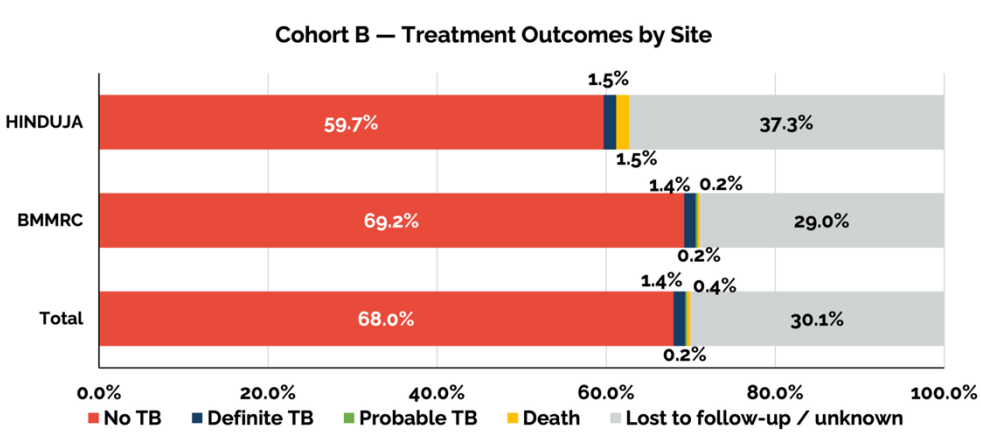
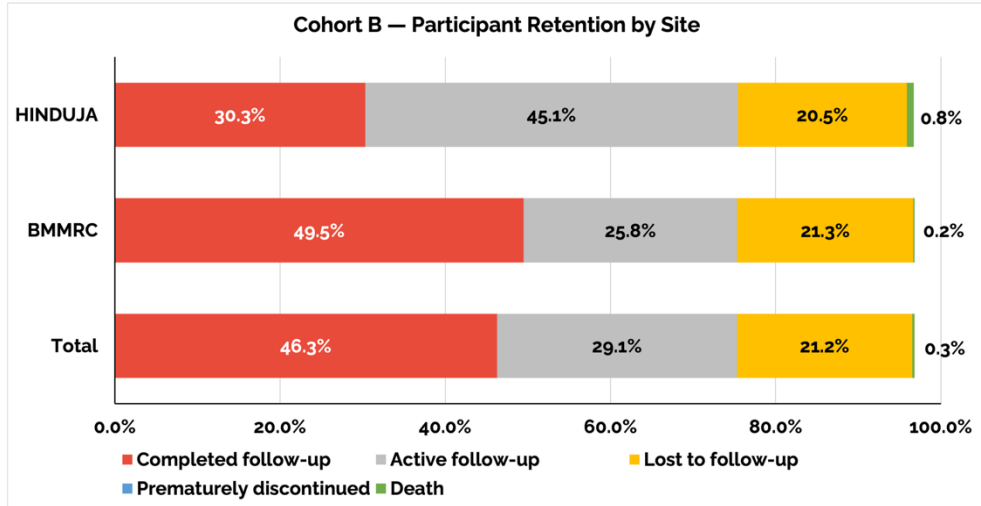
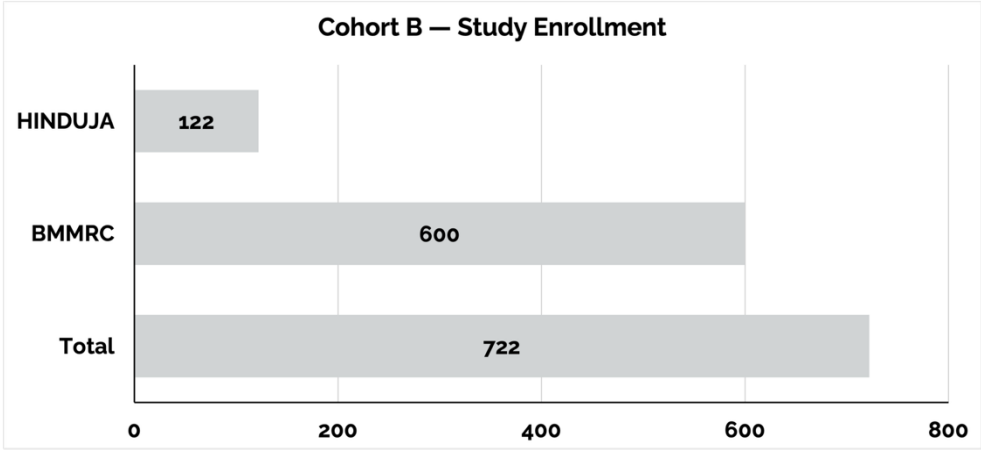


Cohort A Enrollment, Retention, Outcomes & Characteristics



PHASE 2 DATA

Cohort B Enrollment, Retention, Outcomes & Characteristics



RePCORT

INDIA

CONCEPT SHEETS

Resistance to TB Genome-wide Association Study (GWAS)

Lead Investigators: Neel Gandhi, Yan Sun

Institution: Emory University

Submission Date: 8/24/2017

Funding: NIH R01 Awarded

Status: Open - DBT NOC Pending

EC Approval Status: Fully Approved | Initial: 9/25/2017 | Additional Sites: 10/4/2019

CP Data Access: NOC Approved

Action Items: Dec 2020: DBT NOC pending (including additional sites) | Dec 2020: DBT approved TBGWAS NOC

Updates: Study completed; manuscript under review in Nature Communications

Collaboration for NIH IMPAc-TB Contract Application: Immune Responses Associated with Progression to TB

Lead Investigator: Jyothi Rengarajan

Institution: Emory University

Submission Date: 6/20/2018

Funding: NIH Award not funded

EC Approval Status: Approved (contingent on funding)

Status: Closed

UCSF Proposal for NIH IMPAcTB BAA - Identifying Key Immune Responses Needed for Protection against Mtb and for the Development of TB Vaccines

Lead Investigators: Joel Ernst, Adithya Cattamanchi, Payam Nahid

Institution: University of California, San Francisco

Submission Date: 6/26/2018

Funding: NIH Award not funded

EC Approval Status: Approved (contingent on funding)

Status: Closed

RePORT Xpert TB Host Response RUO

Lead Investigator: Robert W. Kwiatkowski

Institution: CEPHEID

Submission Date: 3/5/2019

Funding: Self-funded

Status: Closed- No longer pursuing

EC Approval Status: Initial Review Complete, Awaiting Revised CS

Action Items: RePORT India Pls involved to revise concept sheet and submit for EC/WG review (March) | EC/WG to review revised concept sheet (March/April)

Updates: Sept 2020: Concept sheet submission in progress, specimen availability confirmation and final number of samples based on sample availability across sites to be finalized.

CONCEPT SHEETS

Impact of Nutrition on TB Outcomes (INTO study)

Lead Investigators: Natasha S Hochberg, Padma Chandrasekaran

Institutions: Boston Medical Center and NIRT

Submission Date: 5/14/2019

Funding: N/A (Analysis only)

Status: Open - Analysis Ongoing

EC Approval Status: Fully Approved (4/8/2020)

CP Data Access: Requested: 6/13/2020 | Granted: 7/15/2020

Action Items: Dec 2020: Drs Ponnuraja, Sinha, Hochberg to complete data analysis.

Updates:

- Dec 2020: Analysis Ongoing
- Sept 2020: PP Data granted. They have their analytical plan sketched out with Dr. Padma, Dr. Ponnuraja, Nikhil, Natasha, and Dr. Pranay.
- They are awaiting some missing variables from the SAS team and can then begin data analysis.
- April 2020: DBT has approved Concept sheet inclusive of Indian participants on 8th April. Access for data granted by all participating PIs from Phase I.
- July 2020: Access to CP data has been sent to SAS CHRD on 13th June 2020. SAS has shared the data with the team on 15th July. Awaiting PP data confirmation by the team.
- Oct 2020: SAS sent data elements.
- Nov 2020: Response from SAS: They checked the list of variables for the concept sheet#6 and these diabetes variables were not mentioned in the list, if the team wants data of these diabetes variables, they need to update the concept sheet#6 and get it approved from DBT and EC.
- Dec 2020: Dr. Pranay is currently working on the variables in the PP data. They will make the request for additional variables in the CP dataset just in case they need something more than just the diabetes variables.
- Dec 2020: Dr. Sonali has requested DBT to authorise SAS to release the data as requested by the team (diabetes element). Awaiting response from SAS.

Immune Responses and Effect of Disulfiram on MTB Infected PBMCs as a Potential Host Directed Therapy

Lead Investigators: Amit Singhal, Ramandeep Singh

Institutions: THSTI

Submission Date: 9/26/2019

Funding: Self-funded

EC Approval Status: Fully Approved (2/25/2020)

CP Sample Access: Awaiting THSTI investigators to complete & sign Sample Request Form & MTA

Action Items: Dec 2020: THSTI signature on Sample Request Form and MTA

Status: Study not proceeding due to COVID pandemic

Updates:

- Sept 2020: Concept sheet approved by EC in Feb 2020. Revised protocol with CP samples included approved at BJMC IRB in March 2020, awaiting approval from NIRT and THSTI. Final MTA between THSTI and NIRT Central repository to be signed. Will initiate sample shipments after IRB approvals and MTA signed.
- Dec 2020: NIRT IEC submission for 19th December 2020 in Progress, IRB approval for revised version of the protocol at THSTI unknown (awaiting response from THSTI), NIRT CR will sign the MTA after THSTI completes their signatures. Samples are identified and the CR is aware of the sample list. Once the MTA process completes, sample should be ready to be shipped.

Description of Radiological Involvement and Correlation with Disease Severity Variables & Outcomes

Lead Investigators: DJ Christopher, Bala Thangakunam

Institution: CMC Vellore

Submission Date: 3/24/2021

Funding: CP existing budget will be used

EC Approval Status: Fully Approved (10-06-21)

Status: Data extraction completed and analysis ongoing

Factors Associated with Favorable and Unfavorable Treatment Outcomes among Pulmonary Tuberculosis Patients in South India

Lead Investigators: Senbagavalli Prakash Babu, Sonali Sarkar

Institutions: JIPMER

Submission Date: 5/27/2021

Funding: Funds from the Common Protocol budget will be used to support these efforts

EC Approval Status: Fully Approved

Status: Complete and published

Understanding Mycobacterium tuberculosis Mediated Host Metabolomics in Pulmonary Tuberculosis: Correlation with Disease Severity and Treatment Course

Lead Investigators: Senbagavalli Prakash Babu, Sonali Sarkar

Institutions: JIPMER

Submission Date: 9/9/2021

Funding: Partnerships For Enhanced Engagement in Research (PEER) Women in Science SEED Grants 202

EC Approval Status: Fully Approved

Status: Complete and published

Innovative Modelling for Predicting TB Treatment Outcomes in Global Cohorts

Lead Investigator: Sonya Krishnan

Institutions: JHU

Funding: NIH/CRDF - TB RICG Grant

EC Approval Status: Fully Approved

Status: Manuscript completed

Population Attributable Fractions for TB Disease and Unfavorable TB Treatment Outcomes among TB Cases and their Household Contacts in RePORT India

Lead Investigators: Akshay Gupte, Sonali Sarkar, Natasha Hochberg, Nikhil Gupte, Pranay Sinha

Institutions: JHU, JIPMER, Boston University, BJMC-JHU

Funding: Not related to an existing grant; No RePORT funds will be used

EC Approval Status: Fully Approved

Status: Completed and published

Psychological Distress Among TB Patients and their Household Contacts

Lead Investigator: Nishi Suryavanshi

Institution: BJGMC

Status: Data Incomplete, not proceeding

Analysis of Host Biomarkers Associated with Adverse TB Treatment Outcomes across RePORT International Sites

Lead Investigator: Padmini Salgame

Institution: Rutgers

EC Approval Status: Approved 1/12/2023

Status: RICC Biomarker Study, Analysis underway

Current Status: All transcriptomics assays completed and data analysis underway. Serum-based biomarkers analysis of the RePORT India samples is underway at BJGMC

Validation of Differentially Expressed Monocyte Genes_NIRT

Lead Investigator: Uma Devi

Institution: NIRT

Status: Approved - LOS given

Updates: Repository samples were shipped to Theracues for RNA extraction. The extracted samples have been pending return for validation for an extended period. Requested the release of the samples from Theracues to NIRT for experimental analysis.

Whole Genome Sequencing of MTB Clinical Strains for Determining Drug Resistance and Strain Lineage in India: A Structured Nationwide Approach

Lead Investigator: Sonali Sarkar

Institution: JIPMER

Submission Date: 1/18/2024

Funding: Part of an already approved grant with the involvement of only Indian funding

Status: Approved

EC Approval Status: Part of an already approved grant with the involvement of only Indian funding

Updates: This is part of the InTGS study and analysis is ongoing

Metabolites, Inflammation, Type 2 Diabetes Mellitus and Tuberculosis Patients

Lead Investigator: N. Pavan Kumar

Institution: NIRT

Submission Date: 11/4/2024

Funding: RICC Cross Consortium

EC Approval Status: Approve LOS

Updates: Plasma, PaxGene, and PBMC samples have been received from the RePORT India Central Biorepository, and inflammatory immune profiling and metabolomics assays have been completed. Single-cell RNA sequencing and TB antigen-specific cellular immune response analyses are currently in progress.

Impact of Alcohol Consumption on Tuberculosis Severity, Treatment Response, and Outcomes: A Longitudinal Analysis of AUDIT-C Categories

Lead Investigator: Spurthi Kodali

Institutions: JHU

Submission Date: 2/15/2025

Funding: Common Protocol Budget

EC Approval Status: Approved

Status: Manuscript Submitted

Neutrophil-to-lymphocyte Ratio and Post-tuberculosis Pulmonary Function

Lead Investigator: Jacqueline Dinh

Institution: Boston University

Submission Date: 2/14/2025

Funding: BUMC Fellowship Program

EC Approval Status: Approved

Status: Analysis Underway

The Burden of Anemia in Tuberculosis Progression

Lead Investigator: Sonali Sarkar

Institution: JIPMER

Submission Date: 6/3/2025

Funding: Internal Funding

EC Approval Status: Fully Approved

Status: Manuscript Underway

Impact of Latent TB Infection and Trained Immunity on Susceptibility to SARS-CoV-2 Infection in India

Lead Investigator: Prakash Babu Narasimhan

Institution: JIPMER

Submission Date: 4/28/2025

Funding: A separate budget not related to RePORT will fund these efforts

EC Approval Status: Approved - LOS given

Status: Samples received. Laboratory assays were delayed due to the unavailability of Mtb-LiaSIGHT consumables. Consumables have now been received, and assays are in progress.

Proteomic Discovery of Protein-based TB Recurrence and Death Signatures

Lead Investigator: Sanjeeva Srivastava

Institution: Indian Institute of Technology Bombay

Submission Date: 5/21/2025

Funding: (CRDF) Global Grant Number: 67816

EC Approval Status: Approved

Status: Manuscript under review at iScience

Cohort Representativeness and Country-level Differences among RePORT and leDEA TB-SRN Networks

Lead Investigator: Felipe Ridolfi

Institution: Vanderbilt University Medical Center

Submission Date: 9/6/2025

EC Approval Status: Approved

Status: Approved - LOS given

Variation in Incident Pulmonary TB Risk among Close Contacts in RePORT International

Lead Investigators: Timothy Sterling, Jerry Ellner, Stephany Duda, Felipe Ridolfi

Institution: Vanderbilt University Medical Center

Submission Date: 10/6/2025

Funding: This project will be conducted as part of RICC

EC Approval Status: Awaiting responses regarding DUA

Status: Approved - Awaiting DUA process

Uncovering Co-Infections: Broad PCR Detection of Respiratory Pathogens in Symptomatic TB Patients

Lead Investigator: Sonali Sarkar

Institution: JIPMER

Submission Date: 10/7/2025

Funding: A separate budget not related to RePORT will fund these efforts

EC Approval Status: Approved

Status: PID selection and sample availability checks are complete. Awaiting IRB approval before initiating the CBR sample request

Multiplexed Antigen-Specific Antibody Profiling for Tuberculosis Diagnosis and Biomarker Discovery

Lead Investigator: Rajesh Karyakarte, Camilla Rodrigues, Anirudh Sarkar

Institution: BJGMC

Submission Date: 11/15/2025

Funding: CRDF funds awarded to BJMC site

EC Approval Status: Approved

Status: Approved - LOS given, testing underway

TANTRA - Antigen Development Towards a TB Vaccine Platform

Lead Investigator: Vijaya Valluri, Nimesh Gupta

Institution: BMMRC

Submission Date: 12/3/2025

Funding: A separate budget not related to RePORT will fund these efforts

EC Approval Status: Approved

Status: Approved - LOS given 5/8/2026

Understanding the Molecular and Immunological Correlates of Tuberculosis-induced Cachexia

Lead Investigator: Sonali Sarkar, AneeshKumar Nil

Institution: JIPMER

Submission Date: 12/26/2025

Funding: A separate budget not related to RePORT will fund these efforts

EC Approval Status: Approved

Status: Approved - LOS given

Effects of Ambient and Household Air Pollution and Baseline Mycobacterial Load among Individuals with Tuberculosis

Lead Investigator: Siobhan Carroll

Institution: McGill University

Submission Date: 3/6/2026

Funding: A separate budget not related to RePORT will fund these efforts

EC Approval Status: Approved

Status: Approved - LOS given

Airway Injury Risk Mechanisms and "IL6" (AIR-MAIL)

Lead Investigator: Akshay Gupte

Institution: Boston University

Submission Date: 3/12/2026

Funding: A separate budget not related to RePORT will fund these efforts

EC Status: Approved - LOS given

Status: Approved - LOS given

Agentic AI for RePORT India Data Analysis

Lead Investigator: W. Evan Johnson

Institution: Rutgers University

Submission Date: 4/24/2026

Funding: A separate budget not related to RePORT will fund these efforts

Status: Pending review

Undernutrition-associated Impairment of Biochemical Recovery during Pulmonary Tuberculosis Treatment: A Longitudinal Plasma Metabolomics and Lipidomics Investigation

Lead Investigator: Reuben S. Maghembe

Institution: SFUCHAS, Tanzania

Submission Date: 5/26/2026

Funding: No RePORT India funds requested in this initial draft; independent funding or collaborative laboratory support will be secured before specimen-consuming assays

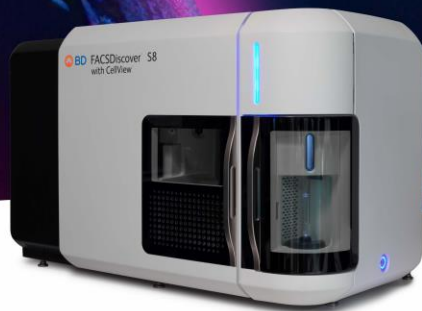
Status: Pending review



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01

Single-Cell & Spatial Omics

- **Single-cell transcriptomics:** 10X Chromium, MGI, ParseBio
- **Spatial transcriptomics:** GeoMx, Visium, Xenium, CosMx, Atera*
- Cell-type annotation, UMAP / t-SNE & clonal mapping
- Cell-cell interaction & spatial biomarker discovery



10X Genomics- Chromium(Single-cell)
Visium HD, Atera*, Bruker GeoMx & CosMX
(Spatial Omics)



02

Bulk Transcriptomics

- **RNA-seq:** Eukaryotic Poly-A, reference-based & *de novo*, bacterial, total RNA, FFPE
- **LongRNA-seq** discovery for isoforms, splice variants & fusions
- **miRNA-seq** differential profiling & integrated miRNA-mRNA analysis
- Host-pathogen **dual RNA-seq** co-expression profiling



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03

Human Genetic Analysis

- **Whole Genome Sequencing** (Germline, RUO) & Research Genome Discovery
- **EXOME:** Standard, Extended & Trio (parent-parent-child)
- Human Mitochondrial DNA & heteroplasmy analysis
- **Human Tumor Panels:** solid, hematologic & fusion RNA



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04

Targeted & Applied Genomics

- Comprehensive **tumor, host-pathogen, lymphoma, leukemia and custom** gene expression panels
- HLA 6-digit typing, STR cell-line typing & ATAC-seq
- **TCR / BCR** repertoire & hybridoma sequencing
- **Transgene & lentiviral** integration characterization



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05

Variant & Diversity Discovery

- Genome-wide discovery of **SNPs, SSRs & repeat markers**
- **Rapid molecular diversity** & population structure analysis
- Cell-line clonality, transgene insertion & identity QC
- **Plasmid & long amplicon** pool long-read sequencing



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06

Metagenomics Solutions

- **16S rRNA profiling:** V3-V4 & full-length whole amplicon
- Whole **metagenome & metatranscriptome** sequencing (ONT)
- Integrated fungal & bacterial microbiome analysis(ONT)
- Microbial / fungal *de novo* genome assembly & resequencing(ONT)



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RePORT

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2026 Conference Book Production Team

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